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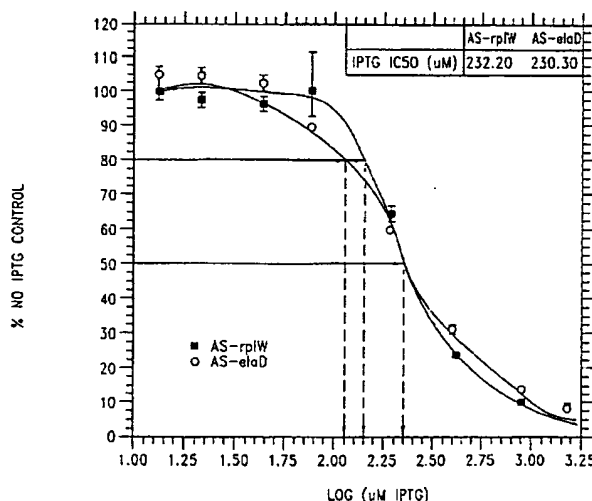
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(54) Title: IDENTIFICATION OF ESSENTIAL GENES IN MICROORGANISMS



(57) Abstract: The sequences of antisense nucleic acids which inhibit the proliferation of prokaryotes are disclosed. Cell-based assays which employ the antisense nucleic acids to identify and develop antibiotics are also disclosed. The antisense nucleic acids can also be used to identify proteins required for proliferation, express these proteins or portions thereof, obtain antibodies capable of specifically binding to the expressed proteins, and to use those expressed proteins as a screen to isolate candidate molecules for rational drug discovery programs. The nucleic acids can also be used to screen for homologous nucleic acids that are required for proliferation in cells other than *Staphylococcus aureus*, *Salmonella typhimurium*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*. The nucleic acids of the present invention can also be used in various assay systems to screen for proliferation required genes in other organisms.

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**IDENTIFICATION OF ESSENTIAL GENES IN MICROORGANISMS**Sequence Listing

The present application is being filed along with quadruplicate copies of a CD-ROM marked "Copy 1 - SEQUENCE LISTING PART," "Copy 2 - SEQUENCE LISTING PART,"  
5 "Copy 3 - SEQUENCE LISTING PART," and "CRF" containing a Sequence Listing in electronic format. The quadruplicate copies of the CD-ROM each contain a file entitled 034VPC\_final.ST25.txt, created on March 15, 2002, which is 181,323,311 bytes in size.

Background of the Invention

Since the discovery of penicillin, the use of antibiotics to treat the ravages of bacterial  
10 infections has saved millions of lives. With the advent of these "miracle drugs," for a time it was popularly believed that humanity might, once and for all, be saved from the scourge of bacterial infections. In fact, during the 1980s and early 1990s, many large pharmaceutical companies cut back or eliminated antibiotics research and development. They believed that infectious disease caused by bacteria finally had been conquered and that markets for new drugs were limited.  
15 Unfortunately, this belief was overly optimistic.

The tide is beginning to turn in favor of the bacteria as reports of drug resistant bacteria become more frequent. The United States Centers for Disease Control announced that one of the most powerful known antibiotics, vancomycin, was unable to treat an infection of the common *Staphylococcus aureus* (staph). This organism is commonly found in our environment and is  
20 responsible for many nosocomial infections. The import of this announcement becomes clear when one considers that vancomycin was used for years to treat infections caused by *Staphylococcus* species as well as other stubborn strains of bacteria. In short, bacteria are becoming resistant to our most powerful antibiotics. If this trend continues, it is conceivable that we will return to a time when what are presently considered minor bacterial infections are fatal diseases.

25 Over-prescription and improper prescription habits by some physicians have caused an indiscriminate increase in the availability of antibiotics to the public. The patients are also partly responsible, since they will often improperly use the drug, thereby generating yet another population of bacteria that is resistant, in whole or in part, to traditional antibiotics.

The bacterial pathogens that have haunted humanity remain, in spite of the development of  
30 modern scientific practices to deal with the diseases that they cause. Drug resistant bacteria are now an increasing threat to the health of humanity. A new generation of antibiotics is needed to once again deal with the pending health threat that bacteria present.

Discovery of New Antibiotics

As more and more bacterial strains become resistant to the panel of available antibiotics,  
35 new antibiotics are required to treat infections. In the past, practitioners of pharmacology would have to rely upon traditional methods of drug discovery to generate novel, safe and efficacious compounds for the treatment of disease. Traditional drug discovery methods involve blindly testing potential drug candidate-molecules, often selected at random, in the hope that one might prove to be

an effective treatment for some disease. The process is painstaking and laborious, with no guarantee of success. Today, the average cost to discover and develop a new drug exceeds US \$500 million, and the average time from laboratory to patient is 15 years. Improving this process, even incrementally, would represent a huge advance in the generation of novel antimicrobial agents.

5 Newly emerging practices in drug discovery utilize a number of biochemical techniques to provide for directed approaches to creating new drugs, rather than discovering them at random. For example, gene sequences and proteins encoded thereby that are required for the proliferation of a cell or microorganism make excellent targets since exposure of bacteria to compounds active against these targets would result in the inactivation of the cell or microorganism. Once a target is  
10 identified, biochemical analysis of that target can be used to discover or to design molecules that interact with and alter the functions of the target. Use of physical and computational techniques to analyze structural and biochemical properties of targets in order to derive compounds that interact with such targets is called rational drug design and offers great potential. Thus, emerging drug discovery practices use molecular modeling techniques, combinatorial chemistry approaches, and  
15 other means to produce and screen and/or design large numbers of candidate compounds.

Nevertheless, while this approach to drug discovery is clearly the way of the future, problems remain. For example, the initial step of identifying molecular targets for investigation can be an extremely time consuming task. It may also be difficult to design molecules that interact with the target by using computer modeling techniques. Furthermore, in cases where the function of the  
20 target is not known or is poorly understood, it may be difficult to design assays to detect molecules that interact with and alter the functions of the target. To improve the rate of novel drug discovery and development, methods of identifying important molecular targets in pathogenic cells or microorganisms and methods for identifying molecules that interact with and alter the functions of such molecular targets are urgently required.

25 *Escherichia coli* represents an excellent model system to understand bacterial biochemistry and physiology. The estimated 4288 genes scattered along the  $4.6 \times 10^6$  base pairs of the *Escherichia coli* (*E. coli*) chromosome offer tremendous promise for the understanding of bacterial biochemical processes. In turn, this knowledge will assist in the development of new tools for the diagnosis and treatment of bacteria-caused human disease. The entire *E. coli* genome has been  
30 sequenced, and this body of information holds a tremendous potential for application to the discovery and development of new antibiotic compounds. Yet, in spite of this accomplishment, the general functions or roles of many of these genes are still unknown. For example, the total number of proliferation-required genes contained within the *E. coli* genome is unknown, but has been variously estimated at around 200 to 700 (Armstrong, K.A. and Fan, D.P. Essential Genes in the  
35 *metB-malB* Region of *Escherichia coli* K12, 1975, J. Bacteriol. 126: 48-55).

*Staphylococcus aureus* is a Gram positive microorganism which is the causative agent of many infectious diseases. Local infection by *Staphylococcus aureus* can cause abscesses on skin and cellulitis in subcutaneous tissues and can lead to toxin-related diseases such as toxic shock and

scalded skin syndromes. *Staphylococcus aureus* can cause serious systemic infections such as osteomyelitis, endocarditis, pneumonia, and septicemia. *Staphylococcus aureus* is also a common cause of food poisoning, often arising from contact between prepared food and infected food industry workers. Antibiotic resistant strains of *Staphylococcus aureus* have recently been identified, including those that are now resistant to all available antibiotics, thereby severely limiting the options of care available to physicians.

*Pseudomonas aeruginosa* is an important Gram negative opportunistic pathogen. It is the most common Gram negative found in nosocomial infections. *P. aeruginosa* is responsible for 16% of nosocomial pneumonia cases, 12% of hospital-acquired urinary tract infections, 8% of surgical wound infections, and 10% of bloodstream infections. Immunocompromised patients, such as neutropenic cancer and bone marrow transplant patients, are particularly susceptible to opportunistic infections. In this group of patients, *P. aeruginosa* is responsible for pneumonia and septicemia with attributable deaths reaching 30%. *P. aeruginosa* is also one of the most common and lethal pathogens responsible for ventilator-associated pneumonia in intubated patients, with directly attributable death rates reaching 38%. Although *P. aeruginosa* outbreaks in burn patients are rare, it is associated with 60% death rates. In the AIDS population, *P. aeruginosa* is associated with 50% of deaths. Cystic fibrosis patients are characteristically susceptible to chronic infection by *P. aeruginosa*, which is responsible for high rates of illness and death. Current antibiotics work poorly for CF infections (Van Delden & Igelwsky. 1998. Emerging Infectious Diseases 4:551-560; references therein).

The gram negative enteric bacterial genus, *Salmonella*, encompasses at least 2 species. One of these, *S. enterica*, is divided into multiple subspecies and thousands of serotypes or serovars (Brenner, et al. 2000 J. Clin. Microbiol. 38:2465-2467). The *S. enterica* human pathogens include serovars Typhi, Paratyphi, Typhimurium, Cholerasuis, and many others deemed so closely related that they are variants of a widespread species. Worldwide, disease in humans caused by *Salmonella* is a very serious problem. In many developing countries, *S. enterica* ser. Typhi still causes often-fatal typhoid fever. This problem has been reduced or eliminated in wealthy industrial states. However, enteritis induced by *Salmonella* is widespread and is the second most common disease caused by contaminated food in the United States (Edwards, BH 1999 "Salmonella and Shigella species" Clin. Lab Med. 19(3):469-487). Though usually self-limiting in healthy individuals, others such as children, seniors, and those with compromising illnesses can be at much greater risk of serious illness and death.

Some *S. enterica* serovars (e.g. Typhimurium) cause a localized infection in the gastrointestinal tract. Other serovars (i.e. Typhi and Paratyphi) cause a much more serious systemic infection. In animal models, these roles can be reversed which has allowed the use of the relatively safe *S. enterica* ser. Typhimurium as a surrogate in mice for the typhoid fever agent, *S. enterica* ser. Typhi. In mice, *S. enterica* ser Typhimurium causes a systemic infection similar in outcome to typhoid fever. Years of study of the *Salmonella* have led to the identification of many determinants

of virulence in animals and humans. *Salmonella* is interesting in its ability to localize to and invade the intestinal epithelium, induce morphologic changes in target cells via injection of certain cell-remodeling proteins, and to reside intracellularly in membrane-bound vesicles (Wallis, TS and Galyov, EE 2000 "Molecular basis of *Salmonella*-induced enteritis." Molec. Microb. 36:997-1005; Falkow, S "The evolution of pathogenicity in *Escherichia*, *Shigella*, and *Salmonella*," Chap. 149 in Neidhardt, et al. eds pp 2723-2729; Gulig, PA "Pathogenesis of Systemic Disease," Chap. 152 in Neidhardt, et al. ppp 2774-2787). The immediate infection often results in a severe watery diarrhea but *Salmonella* also can establish and maintain a subclinical carrier state in some individuals. Spread is via food contaminated with sewage.

10 The gene products implicated in *Salmonella* pathogenesis include type three secretion systems (TTSS), proteins affecting cytoplasmic structure of the target cells, many proteins carrying out functions necessary for survival and proliferation of *Salmonella* in the host, as well as "traditional" factors such as endotoxin and secreted exotoxins. Additionally, there must be factors mediating species-specific illnesses. Despite this most of the genomes of *S. enterica* ser. Typhi (see  
15 [http://www.sanger.ac.uk/Projects/S\\_typhi/](http://www.sanger.ac.uk/Projects/S_typhi/) for the genome database) and *S. enterica* ser. Typhimurium (see <http://genome.wustl.edu/gsc/bacterial/salmonella.shtml> for the genome database) are highly conserved and are mutually useful for gene identification in multiple serovars. The *Salmonella* are a complex group of enteric bacteria causing disease similar to but distinct from other gram negative enterics such as *E. coli* and have been a focus of biomedical research for the  
20 last century.

*Enterococcus faecalis*, a Gram positive bacterium, is by far the most common member of the enterococci to cause infections in humans. *Enterococcus faecium* generally accounts for less than 20% of clinical isolates. Enterococci infections are mostly hospital-acquired though they are also associated with some community-acquired infections. Of nosocomial infections enterococci  
25 account for 12% of bacteremia, 15% of surgical wound infections, 14% of urinary tract infections, and 5 to 15% of endocarditis cases (Huycke, M. M., D. F., Sahm and M. S. Gilmore. 1998. Emerging Infectious Diseases 4:239-249). Additionally enterococci are frequently associated with intraabdominal and pelvic infections. Enterococci infections are often hard to treat because they are resistant to a vast array of antimicrobial drugs, including aminoglycosides, penicillin, ampicillin  
30 and vancomycin. The development of multiple-drug resistant (MDR) enterococci has made this bacteria a major concern for treating nosocomial infections.

Current drug discovery methods involve screening large number of prospective therapeutic compounds to identify those that are effective therapeutic agents or that can be optimized to provide an effective therapeutic agents. For example, the compounds to be evaluated for therapeutic  
35 activity may be members of a library of compounds generated by combinatorial chemistry or members of a library of natural products.

Unfortunately, current methods are laborious and time consuming and may yield compounds which have already been identified or which act on gene products which are already

targeted by an existing therapeutic agent. In addition, a large number of compounds have been identified which have antimicrobial activity but which cannot be administered to individuals suffering from infection due to the fact that their targets are unknown.

The above reasons underscore the urgency of developing new antibiotics that are effective  
5 against *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*,  
*Pseudomonas aeruginosa*, and *Salmonella typhimurium*. Accordingly, there is an urgent need for  
more novel methods to identify and characterize bacterial genomic sequences that encode gene  
products involved in proliferation, and are thereby potential new targets for antibiotic development.  
Likewise, there is a need for rapid screening techniques which yield novel compounds or  
10 compounds which act on novel targets as well as a need for methods which permit the identification  
of the target on which a compound with antimicrobial activity acts.

Prior to the present invention, the discovery of *Escherichia coli*, *Staphylococcus aureus*,  
*Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Salmonella*  
*typhimurium* genes required for proliferation of the microorganism was a painstaking and slow  
15 process. Rapid screening techniques for identifying novel targets on which novel compounds act  
were undeveloped. While the detection and identification of new cellular drug targets within a  
*Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*,  
*Pseudomonas aeruginosa*, and *Salmonella typhimurium* cell is key for novel antibiotic development  
and effective treatment, the current methods of drug target discovery available prior to this  
20 invention have required painstaking processes requiring years of effort.

#### Summary of the Invention

Some aspects of the present invention are described in the numbered paragraphs below.

1. A purified or isolated nucleic acid sequence comprising a nucleotide sequence  
consisting essentially of one of SEQ ID NOs: 1-6213, wherein expression of said nucleic acid  
25 inhibits proliferation of a cell.
2. The nucleic acid sequence of Paragraph 1, wherein said nucleotide sequence is  
complementary to at least a portion of a coding sequence of a gene whose expression is required for  
proliferation of a cell.
3. The nucleic acid of Paragraph 1, wherein said nucleic acid sequence is  
30 complementary to at least a portion of a nucleotide sequence of an RNA required for proliferation  
of a cell.
4. The nucleic acid of Paragraph 3, wherein said RNA is an RNA comprising a  
sequence of nucleotides encoding more than one gene product.
5. A purified or isolated nucleic acid comprising a fragment of one of SEQ ID NOs.:  
35 1-6213, said fragment selected from the group consisting of fragments comprising at least 10, at  
least 20, at least 25, at least 30, at least 50 and more than 50 consecutive nucleotides of one of SEQ  
ID NOs: 1-6213.

6. The fragment of Paragraph 5, wherein said fragment is included in a nucleic acid obtained from an organism selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

7. The fragment of Paragraph 5, wherein said fragment is included in a nucleic acid obtained from an organism other than *Escherichia coli*.

8. A vector comprising a promoter operably linked to the nucleic acid of any one of Paragraphs 1-7.

9. The vector of Paragraph 8, wherein said promoter is active in a microorganism selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*,

- Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*,  
5 *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*,  
10 *Yersinia pestis* and any species falling within the genera of any of the above species.
10. A host cell containing the vector of Paragraph 8 or Paragraph 9.
  11. A purified or isolated antisense nucleic acid comprising a nucleotide sequence complementary to at least a portion of an intragenic sequence, intergenic sequence, sequences spanning at least a portion of two or more genes, 5' noncoding region, or 3' noncoding region  
15 within an operon comprising a proliferation-required gene whose activity or expression is inhibited by an antisense nucleic acid comprising the nucleotide sequence of one of SEQ ID NOs.: 1-6213.
  12. The purified or isolated antisense nucleic acid of Paragraph 11, wherein said antisense nucleic acid is complementary to a nucleic acid from an organism selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*,  
20 *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*,  
25 *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*,  
30 *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*,  
35 *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma*

*urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

13. The purified or isolated antisense nucleic acid of Paragraph 11, wherein said nucleotide sequence is complementary to a nucleotide sequence of a nucleic acid from an organism other than *E. coli*.

14. The purified or isolated antisense nucleic acid of Paragraph 11, wherein said proliferation-required gene comprises a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397.

15. A purified or isolated nucleic acid comprising a nucleotide sequence having at least 70% identity to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 1-6213, fragments comprising at least 25 consecutive nucleotides of SEQ ID NOS.: 1-6213, the nucleotide sequences complementary to SEQ ID NOS.: 1-6213 and the sequences complementary to fragments comprising at least 25 consecutive nucleotides of SEQ ID NOS.: 1-6213 as determined using BLASTN version 2.0 with the default parameters.

16. The purified or isolated nucleic acid of Paragraph 15, wherein said nucleic acid is obtained from an organism selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

17. The nucleic acid of Paragraph 15, wherein said nucleic acid is obtained from an organism other than *E. coli*.



18. A vector comprising a promoter operably linked to a nucleic acid encoding a polypeptide whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence of any one of SEQ ID NOs.: 1-6213.

19. The vector of Paragraph 18, wherein said nucleic acid encoding said polypeptide is  
 5 obtained from an organism selected from the group consisting of *Acinetobacter baumannii*,  
*Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella*  
*pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia*  
*mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis*  
*glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*,  
 10 *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia*  
*pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*,  
*Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*,  
*Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*,  
*Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella*  
 15 *pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*,  
*Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*,  
*Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*,  
*Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*,  
*Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas*  
 20 *syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*,  
*Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*,  
*Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*,  
*Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*,  
*Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia*  
 25 *enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

20. The vector of Paragraph 18, wherein said nucleotide sequence encoding said polypeptide is obtained from an organism other than *E. coli*.

21. A host cell containing the vector of Paragraph 18.

22. The vector of Paragraph 18, wherein said polypeptide comprises a polypeptide  
 30 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 42398-  
 78581.

23. The vector of Paragraph 18, wherein said promoter is operably linked to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397.

24. A purified or isolated polypeptide comprising a polypeptide whose expression is  
 35 inhibited by an antisense nucleic acid comprising a nucleotide sequence of any one of SEQ ID  
 NOs.: 1-6213, or a fragment selected from the group consisting of fragments comprising at least 5,

at least 10, at least 20, at least 30, at least 40, at least 50, at least 60 or more than 60 consecutive amino acids of one of the said polypeptides.

25. The polypeptide of Paragraph 24, wherein said polypeptide comprises an amino acid sequence of any one of SEQ ID NOs.: 42398-78581 or a fragment comprising at least 5, at least 10, at least 20, at least 30, at least 40, at least 50, at least 60 or more than 60 consecutive amino acids of a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42398-78581.

26. The polypeptide of Paragraph 24, wherein said polypeptide is obtained from an organism selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

27. The polypeptide of Paragraph 24, wherein said polypeptide is obtained from an organism other than *E. coli*.

28. A purified or isolated polypeptide comprising a polypeptide having at least 25% amino acid identity to a polypeptide whose expression is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, or at least 25% amino acid identity to a fragment comprising at least 10, at least 20, at least 30, at least 40, at least 50, at least 60 or more than 60 consecutive amino acids of a polypeptide whose expression is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 as determined using FASTA version 3.0t78 with the default parameters.

29. The polypeptide of Paragraph 28, wherein said polypeptide has at least 25% identity to a polypeptide comprising one of SEQ ID NOs: 42398-78581 or at least 25% identity to a fragment comprising at least 5, at least 10, at least 20, at least 30, at least 40, at least 50, at least 60 or more than 60 consecutive amino acids of a polypeptide comprising one of SEQ ID NOs.: 42398-78581 as determined using FASTA version 3.0t78 with the default parameters.

30. The polypeptide of Paragraph 28, wherein said polypeptide is obtained from an organism selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

31. The polypeptide of Paragraph 28, wherein said polypeptide is obtained from an organism other than *E. coli*.

32. An antibody capable of specifically binding the polypeptide of one of Paragraphs 28-31.

33. A method of producing a polypeptide, comprising introducing a vector comprising a promoter operably linked to a nucleic acid comprising a nucleotide sequence encoding a polypeptide whose expression is inhibited by an antisense nucleic acid comprising one of SEQ ID NOs.: 1-6213 into a cell.

34. The method of Paragraph 33, further comprising the step of isolating said polypeptide.

35. The method of Paragraph 33, wherein said polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42398-78581.

36. The method of Paragraph 33, wherein said nucleic acid encoding said polypeptide is obtained from an organism selected from the group consisting of *Acinetobacter baumannii*,  
 5 *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia*  
 10 *pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*,  
 15 *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*,  
 20 *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

25 37. The method of Paragraph 33, wherein said nucleic acid encoding said polypeptide is obtained from an organism other than *E. coli*.

38. The method of Paragraph 33, wherein said promoter is operably linked to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397.

30 39. A method of inhibiting proliferation of a cell in an individual comprising inhibiting the activity or reducing the amount of a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 or inhibiting the activity or reducing the amount of a nucleic acid encoding said gene product.

35 40. The method of Paragraph 39, wherein said method comprises inhibiting said activity or reducing said amount of a gene product in an organism selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*,

*Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*,  
 5 *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*,  
 10 *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*,  
 15 *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

20 41. The method of Paragraph 39, wherein said method comprises inhibiting said activity or reducing said amount of a gene product in an organism other than *E. coli*.

42. The method of Paragraph 39, wherein said gene product is present in an organism other than *E. coli*.

25 43. The method of Paragraph 39, wherein said gene product comprises a polypeptide comprising a sequence selected from the group consisting of SEQ ID NOs.: 42398-78581.

44. A method for identifying a compound which influences the activity of a gene product required for proliferation, said gene product comprising a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, said method comprising:

30 contacting said gene product with a candidate compound; and  
 determining whether said compound influences the activity of said gene product.

45. The method of Paragraph 44, wherein said gene product is from an organism selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*,  
 35 *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*,

- Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*,  
5 *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*,  
10 *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*,  
15 *Yersinia pestis* and any species falling within the genera of any of the above species.
46. The method of Paragraph 44, wherein said gene product is from an organism other than *E. coli*.
47. The method of Paragraph 44, wherein said gene product is a polypeptide and said activity is an enzymatic activity.
- 20 48. The method of Paragraph 44, wherein said gene product is a polypeptide and said activity is a carbon compound catabolism activity.
49. The method of Paragraph 44, wherein said gene product is a polypeptide and said activity is a biosynthetic activity.
50. The method of Paragraph 44, wherein said gene product is a polypeptide and said  
25 activity is a transporter activity.
51. The method of Paragraph 44, wherein said gene product is a polypeptide and said activity is a transcriptional activity.
52. The method of Paragraph 44, wherein said gene product is a polypeptide and said activity is a DNA replication activity.
- 30 53. The method of Paragraph 44, wherein said gene product is a polypeptide and said activity is a cell division activity.
54. The method of Paragraph 44, wherein said gene product is an RNA.
55. The method of Paragraph 44, wherein said gene product is a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42398-  
35 78581.
56. A compound identified using the method of Paragraph 44.
57. A method for identifying a compound or nucleic acid having the ability to reduce the activity or level of a gene product required for proliferation, said gene product comprising a

gene product whose activity or expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, said method comprising:

- (a) contacting a target gene or RNA encoding said gene product with a candidate compound or nucleic acid; and
- (b) measuring an activity of said target.

58. The method of Paragraph 57, wherein said target gene or RNA is from an organism selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

59. The method of Paragraph 57, wherein said target gene or RNA is from an organism other than *E. coli*.

60. The method of Paragraph 57, wherein said gene product is from an organism other than *E. coli*.

61. The method of Paragraph 57, wherein said target is a messenger RNA molecule and said activity is translation of said messenger RNA.

62. The method of Paragraph 57, wherein said target is a messenger RNA molecule and said activity is transcription of a gene encoding said messenger RNA.

63. The method of Paragraph 57, wherein said target is a gene and said activity is transcription of said gene.

64. The method of Paragraph 57, wherein said target is a nontranslated RNA and said activity is processing or folding of said nontranslated RNA or assembly of said nontranslated RNA into a protein/RNA complex.

65. The method of Paragraph 57, wherein said target is a messenger RNA molecule  
5 encoding a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOS.: 42398-78581.

66. The method of Paragraph 57, wherein said target comprises a nucleic acid selected from the group consisting of SEQ ID NOS.: 6214-42397.

67. A compound or nucleic acid identified using the method of Paragraph 57.

10 68. A method for identifying a compound which reduces the activity or level of a gene product required for proliferation of a cell, wherein the activity or expression of said gene product is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 1-6213, said method comprising the steps of:

15 (a) providing a sublethal level of an antisense nucleic acid comprising a nucleotide sequence complementary to a nucleic acid comprising a nucleotide sequence encoding said gene product in a cell to reduce the activity or amount of said gene product in said cell, thereby producing a sensitized cell;

(b) contacting said sensitized cell with a compound; and

20 (c) determining the degree to which said compound inhibits proliferation of said sensitized cell relative to a cell which does not contain said antisense nucleic acid.

69. The method of Paragraph 68, wherein said determining step comprises determining whether said compound inhibits the growth of said sensitized cell to a greater extent than said compound inhibits the growth of a nonsensitized cell.

70. The method of Paragraph 68, wherein said cell is a Gram positive bacterium.

25 71. The method of Paragraph 68, wherein said Gram positive bacterium is selected from the group consisting of *Staphylococcus* species, *Streptococcus* species, *Enterococcus* species, *Mycobacterium* species, *Clostridium* species, and *Bacillus* species.

72. The method of Paragraph 68, wherein said bacterium is *Staphylococcus aureus*.

30 73. The method of Paragraph 72, wherein said *Staphylococcus* species is coagulase negative.

74. The method of Paragraph 72, wherein said bacterium is selected from the group consisting of *Staphylococcus aureus* RN450 and *Staphylococcus aureus* RN4220.

35 75. The method of Paragraph 68, wherein said cell is an organism selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*),



*Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*,  
 5 *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*,  
 10 *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*,  
 15 *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

76. The method of Paragraph 68, wherein said cell is not an *E. coli* cell.

77. The method of Paragraph 68, wherein said gene product is from an organism other than *E. coli*.

20 78. The method of Paragraph 68, wherein said antisense nucleic acid is transcribed from an inducible promoter.

79. The method of Paragraph 68, further comprising the step of contacting said cell with a concentration of inducer which induces transcription of said antisense nucleic acid to a sublethal level.

25 80. The method of Paragraph 68, wherein growth inhibition is measured by monitoring optical density of a culture growth solution.

81. The method of Paragraph 68, wherein said gene product is a polypeptide.

82. The method of Paragraph 81, wherein said polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42398-78581.

30 83. The method of Paragraph 68, wherein said gene product is an RNA.

84. The method of Paragraph 68, wherein nucleic acid encoding said gene product comprises a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397.

85. A compound identified using the method of Paragraph 68.

86. A method for inhibiting cellular proliferation comprising introducing an effective  
 35 amount of a compound with activity against a gene whose activity or expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 or a compound with activity against the product of said gene into a population of cells expressing said gene.

87. The method of Paragraph 86, wherein said compound is an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, or a proliferation-inhibiting portion thereof.

88. The method of Paragraph 86, wherein said proliferation inhibiting portion of one of  
5 SEQ ID NOs.: 1-6213 is a fragment comprising at least 10, at least 20, at least 25, at least 30, at least 50 or more than 51 consecutive nucleotides of one of SEQ ID NOs.: 1-6213.

89. The method of Paragraph 86, wherein said population is a population of Gram positive bacteria.

90. The method of Paragraph 89, wherein said population of Gram positive bacteria is  
10 selected from the group consisting of a population of *Staphylococcus* species, *Streptococcus* species, *Enterococcus* species, *Mycobacterium* species, *Clostridium* species, and *Bacillus* species.

91. The method of Paragraph 86, wherein said population is a population of *Staphylococcus aureus*.

92. The method of Paragraph 91, wherein said population is a population of a  
15 bacterium selected from the group consisting of *Staphylococcus aureus* RN450 and *Staphylococcus aureus* RN4220.

93. The method of Paragraph 86, wherein said population is a population of a bacterium selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*,  
25 *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*,  
35 *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

94. The method of Paragraph 86, wherein said population is a population of an organism other than *E. coli*.

95. The method of Paragraph 86, wherein said product of said gene is from an organism other than *E. coli*.

5 96. The method of Paragraph 86, wherein said gene encodes a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42398-78581.

97. The method of Paragraph 86, wherein said gene comprises a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397.

98. A composition comprising an effective concentration of an antisense nucleic acid  
10 comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, or a proliferation-inhibiting portion thereof in a pharmaceutically acceptable carrier.

99. The composition of Paragraph 98, wherein said proliferation-inhibiting portion of one of SEQ ID NOs.: 1-6213 comprises at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive nucleotides of one of SEQ ID NOs.: 1-6213.

15 100. A method for inhibiting the activity or expression of a gene in an operon required for proliferation wherein the activity or expression of at least one gene in said operon is inhibited by an antisense nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs.: 1-6213, said method comprising contacting a cell in a cell population with an antisense nucleic acid complementary to at least a portion of said operon.

20 101. The method of Paragraph 100, wherein said antisense nucleic acid comprises a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 or a proliferation-inhibiting portion thereof.

102. The method of Paragraph 100, wherein said cell is selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*,  
30 *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*,  
35 *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*,

*Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

103. The method of Paragraph 100, wherein said cell is not an *E. coli* cell.
104. The method of Paragraph 100, wherein said gene is from an organism other than *E. coli*.
105. The method of Paragraph 100, wherein said cell is contacted with said antisense nucleic acid by introducing a plasmid which expresses said antisense nucleic acid into said cell population.
106. The method of Paragraph 100, wherein said cell is contacted with said antisense nucleic acid by introducing a phage which encodes said antisense nucleic acid into said cell population.
107. The method of Paragraph 100, wherein said cell is contacted with said antisense nucleic acid by expressing said antisense nucleic acid from the chromosome of cells in said cell population.
108. The method of Paragraph 100, wherein said cell is contacted with said antisense nucleic acid by introducing a promoter adjacent to a chromosomal copy of said antisense nucleic acid such that said promoter directs the transcription of said antisense nucleic acid.
109. The method of Paragraph 100, wherein said cell is contacted with said antisense nucleic acid by introducing a retron which expresses said antisense nucleic acid into said cell population.
110. The method of Paragraph 100, wherein said cell is contacted with said antisense nucleic acid by introducing a ribozyme into said cell-population, wherein a binding portion of said ribozyme comprises said antisense nucleic acid.
111. The method of Paragraph 100, wherein said cell is contacted with said antisense nucleic acid by introducing a liposome comprising said antisense nucleic acid into said cell.
112. The method of Paragraph 100, wherein said cell is contacted with said antisense nucleic acid by electroporation of said antisense nucleic acid into said cell.
113. The method of Paragraph 100, wherein said antisense nucleic acid is a fragment comprising at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive nucleotides of one of SEQ ID NOS.: 1-6213.
114. The method of Paragraph 100 wherein said antisense nucleic acid is a synthetic oligonucleotide.
115. The method of Paragraph 100, wherein said gene comprises a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397.

116. A method for identifying a gene which is required for proliferation of a cell comprising:

- (a) contacting a cell with an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, wherein said cell is a cell other than the organism from which said nucleic acid was obtained;
- (b) determining whether said nucleic acid inhibits proliferation of said cell; and
- (c) identifying the gene in said cell which encodes the mRNA which is complementary to said antisense nucleic acid or a portion thereof.

117. The method of Paragraph 116, wherein said cell is selected from the group consisting of *Staphylococcus* species, *Streptococcus* species, *Enterococcus* species, *Mycobacterium* species, *Clostridium* species, and *Bacillus* species.

118. The method of Paragraph 116 wherein said cell is selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

119. The method of Paragraph 116, wherein said cell is not *E. coli*.

120. The method of Paragraph 116, further comprising operably linking said antisense nucleic acid to a promoter which is functional in said cell, said promoter being included in a vector, and introducing said vector into said cell.

121. A method for identifying a compound having the ability to inhibit proliferation of a cell comprising:

(a) identifying a homolog of a gene or gene product whose activity or level is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs. 1-6213 in a test cell, wherein said test cell is not the cell from which said nucleic acid was obtained;

(b) identifying an inhibitory nucleic acid sequence which inhibits the activity of said homolog in said test cell;

(c) contacting said test cell with a sublethal level of said inhibitory nucleic acid, thus sensitizing said cell;

(d) contacting the sensitized cell of step (c) with a compound; and

(e) determining the degree to which said compound inhibits proliferation of said sensitized cell relative to a cell which does not contain said inhibitory nucleic acid.

122. The method of Paragraph 121, wherein said determining step comprises determining whether said compound inhibits proliferation of said sensitized test cell to a greater extent than said compound inhibits proliferation of a nonsensitized test cell.

123. The method of Paragraph 121, wherein step (a) comprises identifying a nucleic acid homologous to a gene or gene product whose activity or level is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOs. 1-6213 or a nucleic acid encoding a homologous polypeptide to a polypeptide whose activity or level is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOs. 1-6213 by using an algorithm selected from the group consisting of BLASTN version 2.0 with the default parameters and FASTA version 3.0t78 algorithm with the default parameters to identify said homologous nucleic acid or said nucleic acid encoding a homologous polypeptide in a database.

124. The method of Paragraph 121 wherein said step (a) comprises identifying a homologous nucleic acid or a nucleic acid comprising a sequence of nucleotides encoding a homologous polypeptide by identifying nucleic acids which hybridize to said nucleic acid selected from the group consisting of SEQ ID NOs. 1-6213 or the complement of said nucleic acid selected from the group consisting of SEQ ID NOs. 1-6213.

125. The method of Paragraph 121 wherein step (a) comprises expressing a nucleic acid selected from the group consisting of SEQ ID NOs. 1-6213 in said test cell.

126. The method of Paragraph 121, wherein step (a) comprises identifying a homologous nucleic acid or a nucleic acid encoding a homologous polypeptide in a test cell selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida*

*pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*,  
 5 *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*,  
 10 *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*,  
 15 *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

127. The method of Paragraph 121, wherein step (a) comprises identifying a homologous nucleic acid or a nucleic acid encoding a homologous polypeptide in a test cell other than *E. coli*.

20 128. The method of Paragraph 121, wherein said inhibitory nucleic acid is an antisense nucleic acid.

129. The method of Paragraph 121, wherein said inhibitory nucleic acid comprises an antisense nucleic acid to a portion of said homolog.

25 130. The method of Paragraph 121, wherein said inhibitory nucleic acid comprises an antisense nucleic acid to a portion of the operon encoding said homolog.

131. The method of Paragraph 121, wherein the step of contacting the cell with a sublethal level of said inhibitory nucleic acid comprises directly contacting the surface of said cell with said inhibitory nucleic acid.

30 132. The method of Paragraph 121, wherein the step of contacting the cell with a sublethal level of said inhibitory nucleic acid comprises transcribing an antisense nucleic acid complementary to at least a portion of the RNA transcribed from said homolog in said cell.

133. The method of Paragraph 121, wherein said gene product comprises a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOS.: 42398-78581.

35 134. The method of Paragraph 121, wherein said gene comprises a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397.

135. A compound identified using the method of Paragraph 121.

136. A method of identifying a compound having the ability to inhibit proliferation comprising:

(a) contacting a test cell with a sublethal level of a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs. 1-6213 or a portion thereof which inhibits the proliferation of the cell from which said nucleic acid was obtained, thus sensitizing said test cell;

(b) contacting the sensitized test cell of step (a) with a compound; and

(c) determining the degree to which said compound inhibits proliferation of said sensitized test cell relative to a cell which does not contain said nucleic acid.

137. The method of Paragraph 136, wherein said determining step comprises determining whether said compound inhibits proliferation of said sensitized test cell to a greater extent than said compound inhibits proliferation of a nonsensitized test cell.

138. A compound identified using the method of Paragraph 136.

139. The method of Paragraph 136, wherein said test cell is selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

140. The method of Paragraph 136, wherein the test cell is not *E. coli*.

141. A method for identifying a compound having activity against a biological pathway required for proliferation comprising:



(a) sensitizing a cell by providing a sublethal level of an antisense nucleic acid complementary to a nucleic acid encoding a gene product required for proliferation, wherein the activity or expression of said gene product is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID

NOs.: 1-6213, in said cell to reduce the activity or amount of said gene product;

(b) contacting the sensitized cell with a compound; and

(c) determining the degree to which said compound inhibits the growth of said sensitized cell relative to a cell which does not contain said antisense nucleic acid.

142. The method of Paragraph 141, wherein said determining step comprises determining whether said compound inhibits the growth of said sensitized cell to a greater extent than said compound inhibits the growth of a nonsensitized cell.

143. The method of Paragraph 141, wherein said cell is selected from the group consisting of bacterial cells, fungal cells, plant cells, and animal cells.

144. The method of Paragraph 141, wherein said cell is a Gram positive bacterium.

145. The method of Paragraph 144, wherein said Gram positive bacterium is selected from the group consisting of *Staphylococcus* species, *Streptococcus* species, *Enterococcus* species, *Mycobacterium* species, *Clostridium* species, and *Bacillus* species.

146. The method of Paragraph 145, wherein said Gram positive bacterium is *Staphylococcus aureus*.

147. The method of Paragraph 146, wherein said Gram positive bacterium is selected from the group consisting of *Staphylococcus aureus* RN450 and *Staphylococcus aureus* RN4220.

148. The method of Paragraph 141, wherein said cell is selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella*

- typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*,  
5 *Yersinia pestis* and any species falling within the genera of any of the above species.
149. The method of Paragraph 141, wherein said cell is not an *E. coli* cell.
150. The method of Paragraph 141, wherein said gene product is from an organism other than *E. coli*.
151. The method of Paragraph 141, wherein said antisense nucleic acid is transcribed  
10 from an inducible promoter.
152. The method of Paragraph 141, further comprising contacting the cell with an agent which induces transcription of said antisense nucleic acid from said inducible promoter, wherein said antisense nucleic acid is transcribed at a sublethal level.
153. The method of Paragraph 141, wherein inhibition of proliferation is measured by  
15 monitoring the optical density of a liquid culture.
154. The method of Paragraph 141, wherein said gene product comprises a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42398-78581.
155. The method of Paragraph 141, wherein said nucleic acid encoding said gene  
20 product comprises a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397.
156. A compound identified using the method of Paragraph 141.
157. A method for identifying a compound having the ability to inhibit cellular proliferation comprising:  
25 (a) contacting a cell with an agent which reduces the activity or level of a gene product required for proliferation of said cell, wherein said gene product is a gene product whose activity or expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213;
- (b) contacting said cell with a compound; and  
30 (c) determining whether said compound reduces proliferation of said contacted cell by acting on said gene product.
158. The method of Paragraph 157, wherein said determining step comprises determining whether said compound reduces proliferation of said contacted cell to a greater extent than said compound reduces proliferation of cells which have not been contacted with said agent.
159. The method of Paragraph 157, wherein said cell is selected from the group  
35 consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida*

*glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*,  
 5 *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*,  
 10 *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*,  
 15 *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

160. The method of Paragraph 157, wherein said cell is not an *E. coli* cell.
- 20 161. The method of Paragraph 157, wherein said gene product is from an organism other than *E. coli*.
162. The method of Paragraph 157, wherein said agent which reduces the activity or level of a gene product required for proliferation of said cell comprises an antisense nucleic acid to a gene or operon required for proliferation.
- 25 163. The method of Paragraph 157, wherein said agent which reduces the activity or level of a gene product required for proliferation of said cell comprises a compound known to inhibit growth or proliferation of a cell.
164. The method of Paragraph 157, wherein said cell contains a mutation which reduces the activity or level of said gene product required for proliferation of said cell.
- 30 165. The method of Paragraph 157, wherein said mutation is a temperature sensitive mutation.
166. The method of Paragraph 157, wherein said gene product comprises a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42398-78581.
- 35 167. A compound identified using the method of Paragraph 157.
168. A method for identifying the biological pathway in which a proliferation-required gene or its gene product lies, wherein said gene or gene product comprises a gene or gene product

whose activity or expression is inhibited by an antisense nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs.: 1-6213, said method comprising:

(a) providing a sublethal level of an antisense nucleic acid which inhibits the activity of said proliferation-required gene or gene product in a test cell;

(b) contacting said test cell with a compound known to inhibit growth or proliferation of a cell, wherein the biological pathway on which said compound acts is known; and

(c) determining the degree to which said proliferation of said test cell is inhibited relative to a cell which was not contacted with said compound.

169. The method of Paragraph 168, wherein said determining step comprises determining whether said test cell has a substantially greater sensitivity to said compound than a cell which does not express said sublethal level of said antisense nucleic acid.

170. The method of Paragraph 168, wherein said gene product comprises a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42398-78581.

171. The method of Paragraph 168, wherein said test cell is selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

172. The method of Paragraph 168, wherein said test cell is not an *E. coli* cell.

173. The method of Paragraph 168, wherein said gene product is from an organism other than *E. coli*.

174. A method for determining the biological pathway on which a test compound acts comprising:

5 (a) providing a sublethal level of an antisense nucleic acid complementary to a proliferation-required nucleic acid in a first cell, wherein the activity or expression of said proliferation-required nucleic acid is inhibited by an antisense nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOs.: 1-6213 and wherein the biological pathway in which said proliferation-required nucleic acid or a protein encoded  
10 by said proliferation-required nucleic acid lies is known,

(b) contacting said first cell with said test compound; and

(c) determining the degree to which said test compound inhibits proliferation of said first cell relative to a cell which does not contain said antisense nucleic acid.

175. The method of Paragraph 174, wherein said determining step comprises  
15 determining whether said first cell has a substantially greater sensitivity to said test compound than a cell which does not express said sublethal level of said antisense nucleic acid.

176. The method of Paragraph 174, further comprising:

(d) providing a sublethal level of a second antisense nucleic acid complementary to a second proliferation-required nucleic acid in a second cell, wherein said second  
20 proliferation-required nucleic acid is in a different biological pathway than said proliferation-required nucleic acid in step (a); and

(e) determining whether said second cell does not have a substantially greater sensitivity to said test compound than a cell which does not express said sublethal level of said second antisense nucleic acid, wherein said test compound is specific for the biological  
25 pathway against which the antisense nucleic acid of step (a) acts if said first cell has a substantially greater sensitivity to said test compound than said second cell.

177. The method of Paragraph 174, wherein said first cell is selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*,  
30 *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*,  
35 *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*,

*Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*,  
5 *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*,  
10 *Yersinia pestis* and any species falling within the genera of any of the above species.

178. The method of Paragraph 174, wherein said first cell is not an *E. coli* cell.

179. The method of Paragraph 174, wherein said proliferation-required nucleic acid is from an organism other than *E. coli*.

180. A purified or isolated nucleic acid comprising a sequence selected from the group  
15 consisting of SEQ ID NOs.: 1-6213.

181. A compound which interacts with a gene or gene product whose activity or expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence of one of SEQ ID NOs.: 1-6213 to inhibit proliferation.

182. The compound of Paragraph 181, wherein said gene product is a polypeptide  
20 comprising one of SEQ ID NOs.: 42398-78581.

183. The compound of Paragraph 181, wherein said gene comprises a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397.

184. A compound which interacts with a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence of one of SEQ ID NOs.: 1-6213 to  
25 inhibit proliferation.

185. A method for manufacturing an antibiotic comprising the steps of:  
screening one or more candidate compounds to identify a compound that reduces the activity or level of a gene product required for proliferation, said gene product comprising a gene product whose activity or expression is inhibited by an antisense nucleic acid comprising a  
30 nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213; and  
manufacturing the compound so identified.

186. The method of Paragraph 185, wherein said screening step comprises performing any one of the methods of Paragraphs 44, 68, 121, 136, 141, and 157.

187. The method of Paragraph 185, wherein said gene product is a polypeptide  
35 comprising one of SEQ ID NOs.: 42398-78581.

188. A method for inhibiting proliferation of a cell in a subject comprising administering an effective amount of a compound that reduces the activity or level of a gene product required for proliferation of said cell, said gene product comprising a gene product whose activity or expression

is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 to said subject.

189. The method of Paragraph 188 wherein said subject is selected from the group consisting of vertebrates, mammals, avians, and human beings.

190. The method of Paragraph 188, wherein said gene product comprises a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42398-78581.

191. The method of Paragraph 188, wherein said cell is selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

192. The method of Paragraph 188, wherein said cell is not *E. coli*.

193. The method of Paragraph 188, wherein said gene product is from an organism other than *E. coli*.

194. A purified or isolated nucleic acid consisting essentially of the coding sequence of one of SEQ ID NOs: 6214-42397.

195. A fragment of the nucleic acid of Paragraph 8, said fragment comprising at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive nucleotides of one of SEQ ID NOs: 6214-42397.

196. A purified or isolated nucleic acid comprising a nucleic acid having at least 70% nucleotide sequence identity to a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 6214-42397, fragments comprising at least 25 consecutive nucleotides of SEQ ID NOs.: 6214-42397, the nucleotide sequences complementary to SEQ ID NOs.: 6214-42397, and the  
 5 nucleotide sequences complementary to fragments comprising at least 25 consecutive nucleotides of SEQ ID NOs.: 6214-42397 as determined using BLASTN version 2.0 with the default parameters.

197. The nucleic acid of Paragraph 196, wherein said nucleic acid is from an organism selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*,  
 10 *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*,  
 15 *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*,  
 20 *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*,  
 25 *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

30 198. The nucleic acid of Paragraph 196, wherein said nucleic acid is from an organism other than *E. coli*.

199. A method of inhibiting proliferation of a cell comprising inhibiting the activity or reducing the amount of a gene product in said cell or inhibiting the activity or reducing the amount of a nucleic acid encoding said gene product in said cell, wherein said gene product is selected from  
 35 the group consisting of a gene product having having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid having at



least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs: 1-6213, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs: 1-6213, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs: 1-6213 under stringent conditions, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs: 1-6213 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs: 1-6213.

200. The method of Paragraph 199, wherein said method comprises inhibiting said activity or reducing said amount of said gene product or inhibiting the activity or reducing the amount of a nucleic acid encoding said gene product in an organism selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

201. The method of Paragraph 199, wherein said method comprises inhibiting said activity or reducing said amount of said gene product or inhibiting the activity or reducing the amount of a nucleic acid encoding said gene product in an organism other than *E. coli*.

202. The method of Paragraph 199, wherein said gene product is from an organism other  
5 than *E. coli*.

203. The method of Paragraph 199, wherein said gene product comprises a polypeptide selected from the group consisting of a polypeptide having at least 25% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide selected from the group consisting of SEQ ID NOs.: 42398-78581 and a polypeptide whose activity may be complemented by a  
10 polypeptide selected from the group consisting of SEQ ID NOs.: 42398-78581.

204. The method of Paragraph 199, wherein said gene product is encoded by a nucleic acid selected from the group consisting of a nucleic acid comprising a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-  
15 42397, a nucleic acid comprising a nucleotide sequence which hybridizes to a sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under stringent conditions, and a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under moderate conditions.

205. A method for identifying a compound which influences the activity of a gene  
20 product required for proliferation comprising:

contacting a candidate compound with a gene product selected from the group consisting of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the  
25 group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product having at least 25% amino acid  
30 identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 1-6213 under stringent  
35 conditions, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 1-6213 under moderate conditions, and a gene product whose activity may be complemented

by the gene product whose activity is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOs: 1-6213; and

determining whether said candidate compound influences the activity of said gene product.

5           206. The method of Paragraph 205, wherein said gene product is from an organism selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*,  
10 *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*,  
15 *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*,  
20 *Yersinia pestis* and any species falling within the genera of any of the above species.

207. The method of Paragraph 205, wherein said gene product is from an organism other than *E. coli*.

208. The method of Paragraph 205, wherein said gene product is a polypeptide selected  
30 from the group consisting of a polypeptide having at least 25% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide selected from the group consisting of SEQ ID NOs.: 42398-78581 and a polypeptide whose activity may be complemented by a polypeptide selected from the group consisting of SEQ ID NOs: 42398-78581.

209. The method of Paragraph 205, wherein said gene product is encoded by a nucleic  
35 acid selected from the group consisting of a nucleic acid comprising a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397, a nucleic acid which hybridizes to a sequence selected from the group consisting of SEQ ID

NOS.: 6214-42397 under stringent conditions, and a nucleic acid which hybridizes to a sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under moderate conditions.

210. A compound identified using the method of Paragraph 205.

211. A method for identifying a compound or nucleic acid having the ability to reduce  
5 the activity or level of a gene product required for proliferation comprising:

(a) providing a target that is a gene or RNA, wherein said target comprises a nucleic acid that encodes a gene product selected from the group consisting of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is  
10 inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 1-6213, a gene product encoded by a nucleic acid having at least 70% nucleic acid identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group  
15 consisting of SEQ ID NOS.: 1-6213, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a sequence selected from the group consisting of SEQ ID NOS.: 1-6213, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOS.: 1-6213 under stringent conditions, a gene product  
20 encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOS.: 1-6213 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid selected from the group consisting of SEQ ID  
25 NOS.: 1-6213;

(b) contacting said target with a candidate compound or nucleic acid; and

(c) measuring an activity of said target.

212. The method of Paragraph 211, wherein said target gene or RNA is from an organism selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*,  
30 *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*,  
35 *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*,

*Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*,  
 5 *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*,  
 10 *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

213. The method of Paragraph 211, wherein said target gene or RNA is from an organism other than *E. coli*.

214. The method of Paragraph 211, wherein said gene product is from an organism other  
 15 than *E. coli*.

215. The method of Paragraph 211, wherein said target is a messenger RNA molecule and said activity is translation of said messenger RNA.

216. The method of Paragraph 211, wherein said compound is a nucleic acid and said activity is translation of said gene product.

20 217. The method of Paragraph 211, wherein said target is a gene and said activity is transcription of said gene.

218. The method of Paragraph 211, wherein said target is a nontranslated RNA and said activity is processing or folding of said nontranslated RNA or assembly of said nontranslated RNA into a protein/RNA complex.

25 219. The method of Paragraph 211, wherein said target gene is a messenger RNA molecule encoding a polypeptide selected from the group consisting of a polypeptide having at least 25% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide selected from the group consisting of SEQ ID NOS.: 42398-78581 and a polypeptide whose activity may be complemented by a polypeptide selected from the group consisting of SEQ ID NOS.: 42398-78581.

30 220. The method of Paragraph 11, wherein said target gene comprises a nucleic acid selected from the group consisting of a nucleic acid comprising a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397, a nucleic acid which hybridizes to a sequence selected from the group consisting of SEQ ID NOS.:  
 35 6214-42397 under stringent conditions, and a nucleic acid which hybridizes to a sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under moderate conditions.

221. A compound or nucleic acid identified using the method of Paragraph 211.

222. A method for identifying a compound which reduces the activity or level of a gene product required for proliferation of a cell comprising:

5 (a) providing a sublethal level of an antisense nucleic acid complementary to a nucleic acid encoding said gene product in a cell to reduce the activity or amount of said gene product in said cell, thereby producing a sensitized cell, wherein said gene product is selected from the group consisting of a gene product having having at least 70% nucleic acid identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as  
10 determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited  
15 by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 1-6213 under stringent conditions, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid comprising a  
20 nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOs.: 1-6213;

25 (b) contacting said sensitized cell with a compound; and

(c) determining the degree to which said compound inhibits the growth of said sensitized cell relative to a cell which does not contain said antisense nucleic acid.

223. The method of Paragraph 222, wherein said determining step comprises determining whether said compound inhibits the growth of said sensitized cell to a greater extent  
30 than said compound inhibits the growth of a nonsensitized cell.

224. The method of Paragraph 222, wherein said sensitized cell is a Gram positive bacterium.

225. The method of Paragraph 224, wherein said Gram positive bacterium is selected from the group consisting of *Staphylococcus* species, *Streptococcus* species, *Enterococcus* species,  
35 *Mycobacterium* species, *Clostridium* species, and *Bacillus* species.

226. The method of Paragraph 225, wherein said bacterium is *Staphylococcus aureus*.

227. The method of Paragraph 224, wherein said *Staphylococcus* species is coagulase negative.

228. The method of Paragraph 226, wherein said bacterium is selected from the group consisting of *Staphylococcus aureus* RN450 and *Staphylococcus aureus* RN4220.

229. The method of Paragraph 222, wherein said sensitized cell is an organism selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

230. The method of Paragraph 222, wherein said cell is an organism other than *E. coli*.

231. The method of Paragraph 222, wherein said gene product is from an organism other than *E. coli*.

232. The method of Paragraph 222, wherein said antisense nucleic acid is transcribed from an inducible promoter.

233. The method of Paragraph 222, further comprising the step of contacting said cell with a concentration of inducer which induces transcription of said antisense nucleic acid to a sublethal level.

234. The method of Paragraph 222, wherein growth inhibition is measured by monitoring optical density of a culture medium.

235. The method of Paragraph 222, wherein said gene product is a polypeptide.

236. The method of Paragraph 235, wherein said polypeptide comprises a polypeptide selected from the group consisting of a polypeptide having at least 25% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide selected from the group consisting of

SEQ ID NOS.: 42398-78581 and a polypeptide whose activity may be complemented by a polypeptide selected from the group consisting of SEQ ID NOS: 42398-78581.

237. The method of Paragraph 222, wherein said gene product is an RNA.

238. The method of Paragraph 222, wherein said nucleic acid encoding said gene  
5 product comprises a nucleic acid selected from the group consisting of a nucleic acid comprising a nucleic acid having at least 70% nucleic acid identity as determined using BLASTN version 2.0 with the default parameters to a sequence selected from the group consisting of SEQ ID NOS.: 6214-42397, a nucleic acid which hybridizes to a sequence selected from the group consisting of  
10 SEQ ID NOS.: 6214-42397 under stringent conditions, and a nucleic acid which hybridizes to a sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under moderate conditions.

239. A compound identified using the method of Paragraph 222.

240. A method for inhibiting cellular proliferation comprising introducing a compound  
15 with activity against a gene product or a compound with activity against a gene encoding said gene product into a population of cells expressing said gene product, wherein said gene product is selected from the group consisting of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product  
20 whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 1-6213, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited  
25 by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 1-6213, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of  
30 SEQ ID NOS.: 1-6213, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOS.: 1-6213 under stringent conditions, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOS.: 1-6213 under moderate conditions, and a gene product whose activity may be complemented by the  
gene product whose activity is inhibited by a nucleic acid selected from the group consisting of  
SEQ ID NOS: 1-6213.

241. The method of Paragraph 240, wherein said compound is an antisense nucleic acid  
35 comprising a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 1-6213, or a proliferation-inhibiting portion thereof.

242. The method of Paragraph 240, wherein said proliferation inhibiting portion of one  
of SEQ ID NOS.: 1-6213 is a fragment comprising at least 10, at least 20, at least 25, at least 30, at  
least 50 or more than 51 consecutive nucleotides of one of SEQ ID NOS.: 1-6213.



243. The method of Paragraph 240, wherein said population is a population of Gram positive bacteria.

244. The method of Paragraph 243, wherein said population of Gram positive bacteria is selected from the group consisting of a population of *Staphylococcus* species, *Streptococcus* species, *Enterococcus* species, *Mycobacterium* species, *Clostridium* species, and *Bacillus* species.

245. The method of Paragraph 243, wherein said population is a population of *Staphylococcus aureus*.

246. The method of Paragraph 245, wherein said population is a population of a bacterium selected from the group consisting of *Staphylococcus aureus* RN450 and *Staphylococcus aureus* RN4220.

247. The method of Paragraph 240, wherein said population is a population of a bacterium selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefir* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

248. The method of Paragraph 240, wherein said population is a population of an organism other than *E. coli*.

249. The method of Paragraph 240, wherein said product of said gene is from an organism other than *E. coli*.

250. The method of Paragraph 240, wherein said gene product is selected from the group consisting of a polypeptide having at least 25% amino acid identity as determined using

FASTA version 3.0t78 to a polypeptide selected from the group consisting of SEQ ID NOs.: 42398-78581 and a polypeptide whose activity may be complemented by a polypeptide selected from the group consisting of SEQ ID NOs: 42398-78581.

251. The method of Paragraph 240, wherein said gene comprises a nucleic acid selected  
5 from the group consisting of a nucleic acid comprising a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397, a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under stringent conditions, and a nucleic  
10 acid comprising a nucleotide sequence which hybridizes to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under moderate conditions.

252. A preparation comprising an effective concentration of an antisense nucleic acid in a pharmaceutically acceptable carrier wherein said antisense nucleic acid is selected from the group consisting of a nucleic acid comprising a sequence having at least 70% nucleotide sequence identity  
15 as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 or a proliferation-inhibiting portion thereof, a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 1-6213 under stringent conditions, and a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group  
20 consisting of SEQ ID NOs.: 1-6213 under moderate conditions.

253. The preparation of Paragraph 252, wherein said proliferation-inhibiting portion of one of SEQ ID NOs.: 1-6213 comprises at least 10, at least 20, at least 25, at least 30, at least 50 or more than 50 consecutive nucleotides of one of SEQ ID NOs.: 1-6213.

254. A method for inhibiting the activity or expression of a gene in an operon which  
25 encodes a gene product required for proliferation comprising contacting a cell in a cell population with an antisense nucleic acid comprising at least a proliferation-inhibiting portion of said operon in an antisense orientation, wherein said gene product is selected from the group consisting of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic  
30 acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product having at least  
35 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the

group consisting of SEQ ID NOs.: 1-6213 under stringent conditions, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 1-6213 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOs.: 1-6213.

255. The method of Paragraph 254, wherein said antisense nucleic acid comprises a nucleotide sequence having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a proliferation inhibiting portion thereof, a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 1-6213 under stringent conditions, and a nucleic acid which comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 1-6213 under moderate conditions.

256. The method of Paragraph 254, wherein said cell is selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

257. The method of Paragraph 254, wherein said cell is not an *E. coli* cell.

258. The method of Paragraph 254, wherein said gene is from an organism other than *E. coli*.

259. The method of Paragraph 254, wherein said cell is contacted with said antisense nucleic acid by introducing a plasmid which transcribes said antisense nucleic acid into said cell population.

260. The method of Paragraph 254, wherein said cell is contacted with said antisense nucleic acid by introducing a phage which transcribes said antisense nucleic acid into said cell population.

261. The method of Paragraph 254, wherein said cell is contacted with said antisense nucleic acid by transcribing said antisense nucleic acid from the chromosome of cells in said cell population.

262. The method of Paragraph 254, wherein said cell is contacted with said antisense nucleic acid by introducing a promoter adjacent to a chromosomal copy of said antisense nucleic acid such that said promoter directs the synthesis of said antisense nucleic acid.

263. The method of Paragraph 254, wherein said cell is contacted with said antisense nucleic acid by introducing a retron which expresses said antisense nucleic acid into said cell population.

264. The method of Paragraph 254, wherein said cell is contacted with said antisense nucleic acid by introducing a ribozyme into said cell-population, wherein a binding portion of said ribozyme is complementary to said antisense oligonucleotide.

265. The method of Paragraph 254, wherein said cell is contacted with said antisense nucleic acid by introducing a liposome comprising said antisense oligonucleotide into said cell.

266. The method of Paragraph 254, wherein said cell is contacted with said antisense nucleic acid by electroporation of said antisense nucleic acid into said cell.

267. The method of Paragraph 254, wherein said antisense nucleic acid has at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence comprising at least 10, at least 20, at least 25; at least 30, at least 50 or more than 50 consecutive nucleotides of one of SEQ ID NOS.: 1-6213.

268. The method of Paragraph 254 wherein said antisense nucleic acid is a synthetic oligonucleotide.

269. The method of Paragraph 254, wherein said gene comprises a nucleic acid selected from the group consisting of a nucleic acid comprising a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397, a nucleic acid comprising a nucleotide sequence which hybridizes to a sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under stringent conditions, and a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under moderate conditions.

270. A method for identifying a gene which is required for proliferation of a cell comprising:

(a) contacting a cell with an antisense nucleic acid selected from the group consisting of a nucleic acid at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 or a proliferation-inhibiting portion thereof, a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 1-6213 under stringent conditions, and a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 1-6213 under moderate conditions, wherein said cell is a cell other than the organism from which said nucleic acid was obtained;

(b) determining whether said nucleic acid inhibits proliferation of said cell; and

(c) identifying the gene in said cell which encodes the mRNA which is complementary to said antisense nucleic acid or a portion thereof.

271. The method of Paragraph 270, wherein said cell is selected from the group consisting of *Staphylococcus* species, *Streptococcus* species, *Enterococcus* species, *Mycobacterium* species, *Clostridium* species, and *Bacillus* species.

272. The method of Paragraph 270 wherein said cell is selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

273. The method of Paragraph 270, wherein said cell is not *E. coli*.

274. The method of Paragraph 270, further comprising operably linking said antisense nucleic acid to a promoter which is functional in said cell, said promoter being included in a vector, and introducing said vector into said cell.

5 275. A method for identifying a compound having the ability to inhibit proliferation of a cell comprising:

(a) identifying a homolog of a gene or gene product whose activity or level is inhibited by an antisense nucleic acid in a test cell, wherein said test cell is not the microorganism from which the antisense nucleic acid was obtained, wherein said antisense nucleic acid is selected from the group consisting of a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default  
10 parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOs. 1-6213, a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 1-6213 under stringent conditions, and a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected  
15 from the group consisting of SEQ ID NOs.: 1-6213 under moderate conditions;

(b) identifying an inhibitory nucleic acid sequence which inhibits the activity of said homolog in said test cell;

(c) contacting said test cell with a sublethal level of said inhibitory nucleic acid, thus sensitizing said cell;

20 (d) contacting the sensitized cell of step (c) with a compound; and

(e) determining the degree to which said compound inhibits proliferation of said sensitized cell relative to a cell which does not express said inhibitory nucleic acid.

276. The method of Paragraph 275, wherein said determining step comprises determining whether said compound inhibits proliferation of said sensitized test cell to a greater  
25 extent than said compound inhibits proliferation of a nonsensitized test cell.

277. The method of Paragraph 275, wherein step (a) comprises identifying a homologous nucleic acid to a gene or gene product whose activity or level is inhibited by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID  
30 NOs. 1-6213 or a nucleic acid encoding a homologous polypeptide to a polypeptide whose activity or level is inhibited by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOs. 1-6213 by using an algorithm selected from the group consisting of BLASTN version 2.0 with the default parameters and FASTA version 3.0t78  
35 algorithm with the default parameters to identify said homologous nucleic acid or said nucleic acid encoding a homologous polypeptide in a database.

278. The method of Paragraph 275 wherein said step (a) comprises identifying a homologous nucleic acid or a nucleic acid encoding a homologous polypeptide by identifying

nucleic acids comprising nucleotide sequences which hybridize to said nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOs. 1-6213 or the complement of the nucleotide sequence of said nucleic acid selected from the group consisting of SEQ ID NOs. 1-6213.

279. The method of Paragraph 275 wherein step (a) comprises expressing a nucleic acid having at least 70% nucleic acid identity as determined using BLASTN version 2.0 with the default parameters to a sequence selected from the group consisting of SEQ ID NOs. 1-6213 in said test cell.

280. The method of Paragraph 275, wherein step (a) comprises identifying a homologous nucleic acid or a nucleic acid encoding a homologous polypeptide in an test cell selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

281. The method of Paragraph 275, wherein step (a) comprises identifying a homologous nucleic acid or a nucleic acid encoding a homologous polypeptide in a test cell other than *E. coli*.

282. The method of Paragraph 275, wherein said inhibitory nucleic acid is an antisense nucleic acid.

283. The method of Paragraph 275, wherein said inhibitory nucleic acid comprises an antisense nucleic acid to a portion of said homolog.

284. The method of Paragraph 275, wherein said inhibitory nucleic acid comprises an antisense nucleic acid to a portion of the operon encoding said homolog.

5 285. The method of Paragraph 275, wherein the step of contacting the cell with a sublethal level of said inhibitory nucleic acid comprises directly contacting said cell with said inhibitory nucleic acid.

286. The method of Paragraph 275, wherein the step of contacting the cell with a sublethal level of said inhibitory nucleic acid comprises expressing an antisense nucleic acid to said  
10 homolog in said cell.

287. The method of Paragraph 275, wherein said gene product comprises a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOS.: 42398-78581.

288. The method of Paragraph 275, wherein said gene comprises a nucleic acid selected  
15 from the group consisting of a nucleic acid comprising a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a sequence selected from the group consisting of SEQ ID NOS.: 6214-42397, a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under stringent conditions, and a nucleic acid  
20 comprising a nucleotide sequence which hybridizes to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under moderate conditions.

289. A compound identified using the method of Paragraph 275.

290. A method of identifying a compound having the ability to inhibit proliferation comprising:

25 (a) sensitizing a test cell by contacting said test cell with a sublethal level of an antisense nucleic acid, wherein said antisense nucleic acid is selected from the group consisting of a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOS. 1-6213 or a portion thereof which inhibits the  
30 proliferation of the cell from which said nucleic acid was obtained, a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOS.: 1-6213 under stringent conditions, and a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOS.: 1-6213 under moderate conditions;

35 (b) contacting the sensitized test cell of step (a) with a compound; and

(c) determining the degree to which said compound inhibits proliferation of said sensitized test cell relative to a cell which does not contain said antisense nucleic acid.



291. The method of Paragraph 290, wherein said determining step comprises determining whether said compound inhibits proliferation of said sensitized test cell to a greater extent than said compound inhibits proliferation of a nonsensitized test cell.

292. A compound identified using the method of Paragraph 290.

5 293. The method of Paragraph 290, wherein said test cell is selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*,  
10 *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*,  
15 *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*,  
20 *Yersinia pestis* and any species falling within the genera of any of the above species.

294. The method of Paragraph 290, wherein the test cell is not *E. coli*.

295. A method for identifying a compound having activity against a biological pathway required for proliferation comprising:

30 (a) sensitizing a cell by providing a sublethal level of an antisense nucleic acid complementary to a nucleic acid encoding a gene product required for proliferation, wherein said gene product is selected from the group consisting of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic  
35 acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs: 1-6213, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid

comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs: 1-6213, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 1-6213 under stringent conditions, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 1-6213 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOs: 1-6213;

(b) contacting the sensitized cell with a compound; and

(c) determining the extent to which said compound inhibits the growth of said sensitized cell relative to a cell which does not contain said antisense nucleic acid.

296. The method of Paragraph 295, wherein said determining step comprises determining whether said compound inhibits the growth of said sensitized cell to a greater extent than said compound inhibits the growth of a nonsensitized cell.

297. The method of Paragraph 295, wherein said cell is selected from the group consisting of bacterial cells, fungal cells, plant cells, and animal cells.

298. The method of Paragraph 295, wherein said cell is a Gram positive bacterium.

299. The method of Paragraph 298, wherein said Gram positive bacterium is selected from the group consisting of *Staphylococcus* species, *Streptococcus* species, *Enterococcus* species, *Mycobacterium* species, *Clostridium* species, and *Bacillus* species.

300. The method of Paragraph 299, wherein said Gram positive bacterium is *Staphylococcus aureus*.

301. The method of Paragraph 298, wherein said Gram positive bacterium is selected from the group consisting of *Staphylococcus aureus* RN450 and *Staphylococcus aureus* RN4220.

302. The method of Paragraph 295, wherein said cell is selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria*

*monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*,  
 5 *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*,  
 10 *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

303. The method of Paragraph 295, wherein said cell is not an *E. coli* cell.

304. The method of Paragraph 295, wherein said gene product is from an organism other than *E. coli*.

15 305. The method of Paragraph 295, wherein said antisense nucleic acid is transcribed from an inducible promoter.

306. The method of Paragraph 305, further comprising contacting the cell with an agent which induces expression of said antisense nucleic acid from said inducible promoter, wherein said antisense nucleic acid is expressed at a sublethal level.

20 307. The method of Paragraph 295, wherein inhibition of proliferation is measured by monitoring the optical density of a liquid culture.

308. The method of Paragraph 295, wherein said gene product comprises a polypeptide having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a sequence selected from the group consisting of SEQ ID NOS.: 42398-78581.

25 309. The method of Paragraph 295, wherein said nucleic acid encoding said gene product comprises a nucleic acid selected from the group consisting of a nucleic acid comprising a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397, a nucleic acid comprising a nucleotide sequence which hybridizes to  
 30 a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under stringent conditions, and a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under moderate conditions.

310. A compound identified using the method of Paragraph 295.

35 311. A method for identifying a compound having the ability to inhibit cellular proliferation comprising:

(a) contacting a cell with an agent which reduces the activity or level of a gene product required for proliferation of said cell, wherein said gene product is selected from

the group consisting of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 1-6213 under stringent conditions, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 1-6213 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOs.: 1-6213;

(b) contacting said cell with a compound; and

(c) determining the degree to which said compound reduces proliferation of said contacted cell relative to a cell which was not contacted with said agent.

312. The method of Paragraph 311, wherein said determining step comprises determining whether said compound reduces proliferation of said contacted cell to a greater extent than said compound reduces proliferation of cells which have not been contacted with said agent.

313. The method of Paragraph 311, wherein said cell is selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella*

*haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*,  
 5 *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

314. The method of Paragraph 311, wherein said cell is not an *E. coli* cell.

10 315. The method of Paragraph 311, wherein said gene product is from an organism other than *E. coli*.

316. The method of Paragraph 311, wherein said agent which reduces the activity or level of a gene product required for proliferation of said cell comprises an antisense nucleic acid to a gene or operon required for proliferation.

15 317. The method of Paragraph 311, wherein said agent which reduces the activity or level of a gene product required for proliferation of said cell comprises a compound known to inhibit growth or proliferation of a cell.

318. The method of Paragraph 311, wherein said cell contains a mutation which reduces the activity or level of said gene product required for proliferation of said cell.

20 319. The method of Paragraph 311, wherein said mutation is a temperature sensitive mutation.

320. The method of Paragraph 311, wherein said gene product comprises a gene product comprises a polypeptide having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to an amino acid sequence selected from the group  
 25 consisting of SEQ ID NOs.: 42398-78581.

321. A compound identified using the method of Paragraph 311.

322. A method for identifying the biological pathway in which a proliferation-required gene product or a gene encoding a proliferation-required gene product lies comprising:

(a) providing a sublethal level of an antisense nucleic acid which inhibits the  
 30 activity or reduces the level of said gene encoding a proliferation-required gene product or said said proliferation-required gene product in a test cell, wherein said proliferation-required gene product is selected from the group consisting of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.:  
 35 1-6213, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid

comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs: 1-6213, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 1-6213 under stringent conditions, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 1-6213 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOs: 1-6213;

(b) contacting said test cell with a compound known to inhibit growth or proliferation of a cell, wherein the biological pathway on which said compound acts is known; and

(c) determining the degree to which said compound inhibits proliferation of said test cell relative to a cell which does not contain said antisense nucleic acid.

323. The method of Paragraph 322, wherein said determining step comprises determining whether said test cell has a substantially greater sensitivity to said compound than a cell which does not express said sublethal level of said antisense nucleic acid.

324. The method of Paragraph 322, wherein said gene product comprises a polypeptide having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42398-78581.

325. The method of Paragraph 322, wherein said test cell is selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*,

*Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

326. The method of Paragraph 322, wherein said test cell is not an *E. coli* cell.

327. The method of Paragraph 322, wherein said gene product is from an organism other than *E. coli*.

328. A method for determining the biological pathway on which a test compound acts comprising:

(a) providing a sublethal level of an antisense nucleic acid complementary to a proliferation-required nucleic acid in a cell, thereby producing a sensitized cell, wherein said antisense nucleic acid is selected from the group consisting of a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOs:1-6213 or a proliferation-inhibiting portion thereof, a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 1-6213 under stringent conditions, and a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 1-6213 under moderate conditions and wherein the biological pathway in which said proliferation-required nucleic acid or a protein encoded by said proliferation-required polypeptide lies is known,

(b) contacting said cell with said test compound; and

(c) determining the degree to which said compound inhibits proliferation of said sensitized cell relative to a cell which does not contain said antisense nucleic acid.

329. The method of Paragraph 328, wherein said determining step comprises determining whether said sensitized cell has a substantially greater sensitivity to said test compound than a cell which does not express said sublethal level of said antisense nucleic acid.

330. The method of Paragraph 328, further comprising:

(d) providing a sublethal level of a second antisense nucleic acid complementary to a second proliferation-required nucleic acid in a second cell, wherein said second proliferation-required nucleic acid is in a different biological pathway than said proliferation-required nucleic acid in step (a); and

(e) determining whether said second cell does not have a substantially greater sensitivity to said test compound than a cell which does not express said sublethal level of said second antisense nucleic acid, wherein said test compound is specific for the biological

pathway against which the antisense nucleic acid of step (a) acts if said sensitized cell has substantially greater sensitivity to said test compound than said second cell.

331. The method of Paragraph 328, wherein said sensitized cell is selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*,  
 5 *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium*  
 10 *acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*,  
 15 *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella*  
 20 *typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

25 332. The method of Paragraph 328, wherein said sensitized cell is not an *E. coli* cell.

333. The method of Paragraph 328, wherein said proliferation-required nucleic acid is from an organism other than *E. coli*.

334. A compound which inhibits proliferation by interacting with a gene encoding a gene product required for proliferation or with a gene product required for proliferation, wherein  
 30 said gene product is selected from the group consisting of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using  
 35 BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product



whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 1-6213 under stringent conditions, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 1-6213 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOs.: 1-6213.

335. The compound of Paragraph 334, wherein said gene product comprises a polypeptide having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a sequence selected from the group consisting of SEQ ID NOs.: 42398-78581.

336. The compound of Paragraph 334, wherein said gene comprises a nucleic acid selected from the group consisting of a nucleic acid comprising a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397, a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under stringent conditions, and a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under moderate conditions.

337. A method for manufacturing an antibiotic comprising the steps of:  
screening one or more candidate compounds to identify a compound that reduces the activity or level of a gene product required for proliferation wherein said gene product is selected from the group consisting of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 1-6213 under stringent conditions, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 1-6213 under moderate conditions, and a gene product whose activity may be complemented by the

gene product whose activity is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOs: 1-6213 ; and

manufacturing the compound so identified.

338. The method of Paragraph 337, wherein said screening step comprises performing  
5 any one of the methods of Paragraphs 205, 211, 222, 275, 290, 295, 311.

339. The method of Paragraph 337, wherein said gene product comprises a polypeptide having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42398-78581.

10 340. A method for inhibiting proliferation of a cell in a subject comprising administering an effective amount of a compound that reduces the activity or level of a gene product required for proliferation of said cell, wherein said gene product is selected from the group consisting of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213,  
15 a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product having at least  
20 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 1-6213 under stringent conditions, a gene product encoded by a  
25 nucleic acid comprising a nucleotide sequence which hybridizes to a nucleic acid selected from the group consisting of SEQ ID NOs.: 1-6213 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOs: 1-6213.

341. The method of Paragraph 340 wherein said subject is selected from the group  
30 consisting of vertebrates, mammals, avians, and human beings.

342. The method of Paragraph 340, wherein said gene product comprises a polypeptide having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42398-78581.

35 343. The method of Paragraph 340, wherein said cell is selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida*

*glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*,  
 5 *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*,  
 10 *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*,  
 15 *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

344. The method of Paragraph 340, wherein said cell is not *E. coli*.

20 345. The method of Paragraph 340, wherein said gene product is from an organism other than *E. coli*.

346. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

25 obtaining a culture comprising a plurality of strains wherein each strain in said culture overexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product whose activity or level is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 is overexpressed;

30 contacting said culture with a sufficient concentration of said compound to inhibit the proliferation of strains of said organism which do not overexpress said gene product on which said compound acts, such that strains which overexpress said gene product on which said compound acts proliferate more rapidly than strains which do not overexpress said gene product on which said compound acts; and

35 identifying the gene product which is overexpressed in a strain which proliferated more rapidly in said culture.

347. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

obtaining a culture comprising a plurality of strains wherein each strain in said culture overexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 6214-42397 is overexpressed;

contacting said culture with a sufficient concentration of said compound to inhibit the proliferation of strains of said organism which do not overexpress said gene product on which said compound acts, such that strains which overexpress said gene product on which said compound acts proliferate more rapidly than strains which do not overexpress said gene product on which said compound acts; and

identifying the gene product which is overexpressed in a strain which proliferated more rapidly in said culture.

348. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

obtaining a culture comprising a plurality of strains wherein each strain in said culture overexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42938-78581 is overexpressed;

contacting said culture with a sufficient concentration of said compound to inhibit the proliferation of strains of said organism which do not overexpress said gene product on which said compound acts, such that strains which overexpress said gene product on which said compound acts proliferate more rapidly than strains which do not overexpress said gene product on which said compound acts; and

identifying the gene product which is overexpressed in a strain which proliferated more rapidly in said culture.

349. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

obtaining a culture comprising a plurality of strains wherein each strain in said culture overexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product selected from the group consisting of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide

sequence selected from the group consisting of SEQ ID NOs: 1-6213, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs: 1-6213, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs: 1-6213 under stringent conditions, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs: 1-6213 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs: 1-6213 is overexpressed;

contacting said culture with a sufficient concentration of said compound to inhibit the proliferation of strains of said organism which do not overexpress said gene product on which said compound acts, such that strains which overexpress said gene product on which said compound acts proliferate more rapidly than strains which do not overexpress said gene product on which said compound acts; and

identifying the gene product which is overexpressed in a strain which proliferated more rapidly in said culture.

350. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

obtaining a culture comprising a plurality of strains wherein each strain in said culture overexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of a nucleic acid comprising a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397, a nucleic acid comprising a nucleotide sequence which hybridizes to a sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under stringent conditions, and a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under moderate conditions is overexpressed;

contacting said culture with a sufficient concentration of said compound to inhibit the proliferation of strains of said organism which do not overexpress said gene product on which said compound acts, such that strains which overexpress said gene product on which said compound acts proliferate more rapidly than strains which do not overexpress said gene product on which said compound acts; and

identifying the gene product which is overexpressed in a strain which proliferated more rapidly in said culture.

351. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

5 obtaining a culture comprising a plurality of strains wherein each strain in said culture overexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product comprises a polypeptide selected from the group consisting of a polypeptide having at least 25% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide selected from the group consisting of SEQ ID NOs.: 42938-78581 and a polypeptide whose activity may be  
10 complemented by a polypeptide selected from the group consisting of SEQ ID NOs: 42938-78581 is overexpressed;

contacting said culture with a sufficient concentration of said compound to inhibit the proliferation of strains of said organism which do not overexpress said gene product on  
15 which said compound acts, such that strains which overexpress said gene product on which said compound acts proliferate more rapidly than strains which do not overexpress said gene product on which said compound acts; and

identifying the gene product which is overexpressed in a strain which proliferated more rapidly in said culture.

20 352. The method of Paragraph 346, 347, 348, 349, 350 or 351, wherein said culture includes at least one strain which does not overexpresses a gene product which is essential for proliferation of said organism.

353. The method of Paragraph 346, 347, 348, 349, 350 or 351, wherein said strains which overexpress said gene products comprise a nucleic acid encoding said gene product which is  
25 essential for proliferation of said organism operably linked to a regulatable promoter.

354. The method of Paragraph 346, 347, 348, 349, 350 or 351, wherein said strains which overexpress said gene products a nucleic acid encoding said gene product which is essential for proliferation of said organism operably linked to a constitutive promoter.

355. The method of Paragraph 346, 347, 348, 349, 350 or 351, wherein said  
30 identification step comprises determining the nucleotide sequence of a nucleic acid encoding said gene product in said cell which proliferated more rapidly in said culture.

356. The method of Paragraph 346, 347, 348, 349, 350 or 351, wherein said identification step comprises performing an amplification reaction to identify the nucleic acid encoding said gene product in said cell which proliferated more rapidly in said cell culture.

35 357. The method of Paragraph 356, wherein the products of said amplification reaction are labeled with a detectable dye.

358. The method of Paragraph 346, 347, 348, 349, 350 or 351, wherein said identification step comprises performing a hybridization procedure.

359. The method of Paragraph 346, 347, 348, 349, 350 or 351, wherein said identification step comprises contacting a nucleic acid array with a nucleic acid encoding said gene product in said cell which proliferated more rapidly in said cell culture.

5 360. The method of Paragraph 346, 347, 348, 349, 350 or 351, wherein said organism is selected from the group consisting of bacteria, fungi, and protozoa.

361. The method of Paragraph 346, 347, 348, 349, 350 or 351, wherein said culture is a culture of an organism selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*,  
10 *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*,  
15 *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*,  
20 *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

362. The method of Paragraph 346, 347, 348, 349, 350 or 351, wherein said compound is obtained from a library of natural compounds.

30 363. The method of Paragraph 346, 347, 348, 349, 350 or 351, wherein said compound is obtained from a library of synthetic compounds.

364. The method of Paragraph 346, 347, 348, 349, 350 or 351, wherein said compound is present in a crude or partially purified state.

35 365. The method of Paragraph 346, 347, 348, 349, 350 or 351, further comprising determining whether said gene product in said strain which proliferated more rapidly in said culture has a counterpart in at least one other organism.

366. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

obtaining an array of strains on a solid growth medium wherein each strain overexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product whose activity or level is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 is overexpressed;

contacting said array of strains with a sufficient concentration of said compound to inhibit the proliferation of strains of said organism which do not overexpress said gene product on which said compound acts, such that strains which overexpress said gene product on which said compound acts proliferate more rapidly than strains which do not overexpress said gene product on which said compound acts; and

identifying the gene product which is overexpressed in a strain which proliferated more rapidly on said solid medium.

367. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

obtaining an array of strains on a solid growth medium wherein each strain overexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 6214-42397 is overexpressed;

contacting said array of strains with a sufficient concentration of said compound to inhibit the proliferation of strains of said organism which do not overexpress said gene product on which said compound acts, such that strains which overexpress said gene product on which said compound acts proliferate more rapidly than strains which do not overexpress said gene product on which said compound acts; and

identifying the gene product which is overexpressed in a strain which proliferated more rapidly on said solid medium.

368. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

obtaining an array of strains on a solid growth medium wherein each strain overexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42938-78581 is overexpressed;

contacting said array of strains with a sufficient concentration of said compound to inhibit the proliferation of strains of said organism which do not overexpress said gene product on which said compound acts, such that strains which overexpress said gene product on which said compound acts proliferate more rapidly than strains which do not overexpress said gene product on which said compound acts; and



identifying the gene product which is overexpressed in a strain which proliferated more rapidly on said solid medium.

369. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

5 obtaining an array of strains on a solid growth medium wherein each strain overexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product selected from the group consisting of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression  
10 is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the  
15 group consisting of SEQ ID NOs.: 1-6213, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide  
20 sequence selected from the group consisting of SEQ ID NOs.: 1-6213 under stringent conditions, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid comprising a nucleotide  
25 sequence selected from the group consisting of SEQ ID NOs.: 1-6213 is overexpressed;

contacting said array of strains with a sufficient concentration of said compound to inhibit the proliferation of strains of said organism which do not overexpress said gene product on which said compound acts, such that strains which overexpress said gene product on which said compound acts proliferate more rapidly than strains which do not  
30 overexpress said gene product on which said compound acts; and

identifying the gene product which is overexpressed in a strain which proliferated more rapidly on said solid medium.

370. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

35 obtaining an array of strains on a solid growth medium wherein each strain overexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of a nucleic acid

comprising a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397, a nucleic acid comprising a nucleotide sequence which hybridizes to a sequence selected from the group consisting of  
5 SEQ ID NOS.: 6214-42397 under stringent conditions, and a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under moderate conditions is overexpressed;

contacting said array of strains with a sufficient concentration of said compound to inhibit the proliferation of strains of said organism which do not overexpress said gene  
10 product on which said compound acts, such that strains which overexpress said gene product on which said compound acts proliferate more rapidly than strains which do not overexpress said gene product on which said compound acts; and

identifying the gene product which is overexpressed in a strain which proliferated more rapidly on said solid medium.

15 371. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

obtaining an array of strains on a solid growth medium wherein each strain overexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product comprises a polypeptide  
20 selected from the group consisting of a polypeptide having at least 25% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide selected from the group consisting of SEQ ID NOS.: 42938-78581 and a polypeptide whose activity may be complemented by a polypeptide selected from the group consisting of SEQ ID NOS: 42938-78581 is overexpressed;

25 contacting said array of strains with a sufficient concentration of said compound to inhibit the proliferation of strains of said organism which do not overexpress said gene product on which said compound acts, such that strains which overexpress said gene product on which said compound acts proliferate more rapidly than strains which do not overexpress said gene product on which said compound acts; and

30 identifying the gene product which is overexpressed in a strain which proliferated more rapidly on said solid medium.

372. The method of Paragraph 366, 367, 368, 369, 370 or 371, wherein at least one strain in said array does not overexpresses a gene product which is essential for proliferation of said organism.

35 373. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

obtaining a plurality of cultures, wherein each culture comprises a plurality of strains wherein each strain overexpresses a different gene product which is essential for

proliferation of said organism, wherein said culture comprises a strain in which a gene product whose activity or level is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 is overexpressed;

contacting each of said cultures with a different concentration of said compound;

5 and

identifying the gene product which is overexpressed in a strain whose proliferation is inhibited by said compound.

374. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

10 obtaining a plurality of cultures, wherein each culture comprises a plurality of strains wherein each strain overexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 6214-42397 is overexpressed;

15 contacting each of said cultures with a different concentration of said compound; and

identifying the gene product which is overexpressed in a strain whose proliferation is inhibited by said compound.

375. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

20 obtaining a plurality of cultures, wherein each culture comprises a plurality of strains wherein each strain overexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42938-78581 is overexpressed;

25 contacting each of said cultures with a different concentration of said compound; and

identifying the gene product which is overexpressed in a strain whose proliferation is inhibited by said compound.

30 376. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

35 obtaining a plurality of cultures, wherein each culture comprises a plurality of strains wherein each strain overexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product selected from the group consisting of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene

product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs: 1-6213, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 under stringent conditions, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs: 1-6213 is overexpressed;

contacting each of said cultures with a different concentration of said compound;  
and

identifying the gene product which is overexpressed in a strain whose proliferation is inhibited by said compound.

377. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

obtaining a plurality of cultures, wherein each culture comprises a plurality of strains wherein each strain overexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of a nucleic acid comprising a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397, a nucleic acid comprising a nucleotide sequence which hybridizes to a sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under stringent conditions, and a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under moderate conditions is overexpressed;

contacting each of said cultures with a different concentration of said compound;  
and

identifying the gene product which is overexpressed in a strain whose proliferation is inhibited by said compound.

378. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

obtaining a plurality of cultures, wherein each culture comprises a plurality of strains wherein each strain overexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product comprises a polypeptide selected from the group consisting of a polypeptide having at least 25% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide selected from the group consisting of SEQ ID NOs: 42938-78581 and a polypeptide whose activity may be complemented by a polypeptide selected from the group consisting of SEQ ID NOs: 42938-78581 is overexpressed;

contacting each of said cultures with a different concentration of said compound; and

identifying the gene product which is overexpressed in a strain whose proliferation is inhibited by said compound.

379. The method of Paragraph 373, 374, 375, 376, 377 or 378, wherein at least one strain in said plurality of cultures does not overexpress a gene product which is essential for proliferation of said organism.

380. A method of profiling a compound's activity comprising:

performing the method of Paragraph 346 on a first culture using a first compound;

performing the method of Paragraph 346 on a second culture using a second compound; and

comparing the strains identified in said first culture to the strains identified in said second culture.

381. A method of profiling a compound's activity comprising:

performing the method of Paragraph 347 on a first culture using a first compound;

performing the method of Paragraph 347 on a second culture using a second compound; and

comparing the strains identified in said first culture to the strains identified in said second culture.

382. A method of profiling a compound's activity comprising:

performing the method of Paragraph 348 on a first culture using a first compound;

performing the method of Paragraph 348 on a second culture using a second compound; and

comparing the strains identified in said first culture to the strains identified in said second culture.

383. A method of profiling a compound's activity comprising:

performing the method of Paragraph 349 on a first culture using a first compound;

performing the method of Paragraph 349 on a second culture using a second compound; and

comparing the strains identified in said first culture to the strains identified in said second culture.

5 384. A method of profiling a compound's activity comprising:

performing the method of Paragraph 350 on a first culture using a first compound;

performing the method of Paragraph 350 on a second culture using a second compound; and

10 comparing the strains identified in said first culture to the strains identified in said second culture.

385. A method of profiling a compound's activity comprising:

performing the method of Paragraph 351 on a first culture using a first compound;

performing the method of Paragraph 351 on a second culture using a second compound; and

15 comparing the strains identified in said first culture to the strains identified in said second culture.

386. A method of profiling a first compound's activity comprising:

growing an array of strains on a first solid medium comprising said first compound and on a second solid medium comprising a second compound, wherein each strain in said array overexpresses a different gene product which is essential for proliferation of an organism, wherein said culture comprises a strain in which a gene product whose activity or level is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 is overexpressed, and wherein said first compound and said second compound inhibit the proliferation of said organism; and

20 comparing the pattern of strains which grow on said first solid medium with the pattern of strains which grow on said second solid medium.

387. A method of profiling a first compound's activity comprising:

growing an array of strains on a first solid medium comprising said first compound and on a second solid medium comprising a second compound, wherein each strain in said array overexpresses a different gene product which is essential for proliferation of an organism, wherein said culture comprises a strain in which a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 6214-42397 is overexpressed, and wherein said first compound and said second compound inhibit the proliferation of said organism; and

35 comparing the pattern of strains which grow on said first solid medium with the pattern of strains which grow on said second solid medium.

388. A method of profiling a first compound's activity comprising:

growing an array of strains on a first solid medium comprising said first compound and on a second solid medium comprising a second compound, wherein each strain in said array overexpresses a different gene product which is essential for proliferation of an organism, wherein said culture comprises a strain in which a gene product comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42938-78581 is overexpressed, and wherein said first compound and said second compound inhibit the proliferation of said organism; and

comparing the pattern of strains which grow on said first solid medium with the pattern of strains which grow on said second solid medium.

389. A method of profiling a first compound's activity comprising:

growing an array of strains on a first solid medium comprising said first compound and on a second solid medium comprising a second compound, wherein each strain in said array overexpresses a different gene product which is essential for proliferation of an organism, wherein said culture comprises a strain in which a gene product selected from the group consisting of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 under stringent conditions, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 is overexpressed, and wherein said first compound and said second compound inhibit the proliferation of said organism; and

comparing the pattern of strains which grow on said first solid medium with the pattern of strains which grow on said second solid medium.

390. A method of profiling a first compound's activity comprising:

growing an array of strains on a first solid medium comprising said first compound and on a second solid medium comprising a second compound, wherein each strain in said array overexpresses a different gene product which is essential for proliferation of an organism, wherein said culture comprises a strain in which a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of a nucleic acid comprising a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397, a nucleic acid comprising a nucleotide sequence which hybridizes to a sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under stringent conditions, and a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under moderate conditions is overexpressed, and wherein said first compound and said second compound inhibit the proliferation of said organism; and

comparing the pattern of strains which grow on said first solid medium with the pattern of strains which grow on said second solid medium.

391. A method of profiling a first compound's activity comprising:

growing an array of strains on a first solid medium comprising said first compound and on a second solid medium comprising a second compound, wherein each strain in said array overexpresses a different gene product which is essential for proliferation of an organism, wherein said culture comprises a strain in which a gene product comprises a polypeptide selected from the group consisting of a polypeptide having at least 25% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide selected from the group consisting of SEQ ID NOS.: 42938-78581 and a polypeptide whose activity may be complemented by a polypeptide selected from the group consisting of SEQ ID NOS.: 42938-78581 is overexpressed, and wherein said first compound and said second compound inhibit the proliferation of said organism; and

comparing the pattern of strains which grow on said first solid medium with the pattern of strains which grow on said second solid medium.

392. The method of any one of Paragraphs 380, 381, 382, 383, 384, 385, 386, 387, 388, 389, 390 or 391, wherein said first compound is present in a crude or partially purified state.

393. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

obtaining a culture comprising a plurality of strains wherein each strain underexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product whose activity or level is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 1-6213 is underexpressed;



contacting said culture with a sufficient concentration of said compound to inhibit the proliferation of strains of said organism which underexpress said gene product on which said compound acts, such that strains which underexpress said gene product on which said compound acts proliferate more slowly than strains which do not underexpress said gene product on which said compound acts; and

identifying the gene product which is underexpressed in a strain which proliferated more slowly in said culture.

394. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

obtaining a culture comprising a plurality of strains wherein each strain underexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 6214-42397 is underexpressed;

contacting said culture with a sufficient concentration of said compound to inhibit the proliferation of strains of said organism which underexpress said gene product on which said compound acts, such that strains which underexpress said gene product on which said compound acts proliferate more slowly than strains which do not underexpress said gene product on which said compound acts; and

identifying the gene product which is underexpressed in a strain which proliferated more slowly in said culture.

395. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

obtaining a culture comprising a plurality of strains wherein each strain underexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42938-78581 is underexpressed;

contacting said culture with a sufficient concentration of said compound to inhibit the proliferation of strains of said organism which underexpress said gene product on which said compound acts, such that strains which underexpress said gene product on which said compound acts proliferate more slowly than strains which do not underexpress said gene product on which said compound acts; and

identifying the gene product which is underexpressed in a strain which proliferated more slowly in said culture.

396. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

obtaining a culture comprising a plurality of strains wherein each strain underexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product selected from the group consisting of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 under stringent conditions, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 is underexpressed;

contacting said culture with a sufficient concentration of said compound to inhibit the proliferation of strains of said organism which underexpress said gene product on which said compound acts, such that strains which underexpress said gene product on which said compound acts proliferate more slowly than strains which do not underexpress said gene product on which said compound acts; and

identifying the gene product which is underexpressed in a strain which proliferated more slowly in said culture.

397. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

obtaining a culture comprising a plurality of strains wherein each strain underexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of a nucleic acid comprising a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397, a nucleic acid

comprising a nucleotide sequence which hybridizes to a sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under stringent conditions, and a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under moderate conditions is underexpressed;

contacting said culture with a sufficient concentration of said compound to inhibit the proliferation of strains of said organism which underexpress said gene product on which said compound acts, such that strains which underexpress said gene product on which said compound acts proliferate more slowly than strains which do not underexpress said gene product on which said compound acts; and

identifying the gene product which is underexpressed in a strain which proliferated more slowly in said culture.

398. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

obtaining a culture comprising a plurality of strains wherein each strain underexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product comprises a polypeptide selected from the group consisting of a polypeptide having at least 25% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide selected from the group consisting of SEQ ID NOS.: 42938-78581 and a polypeptide whose activity may be complemented by a polypeptide selected from the group consisting of SEQ ID NOS: 42938-78581 is underexpressed;

contacting said culture with a sufficient concentration of said compound to inhibit the proliferation of strains of said organism which underexpress said gene product on which said compound acts, such that strains which underexpress said gene product on which said compound acts proliferate more slowly than strains which do not underexpress said gene product on which said compound acts; and

identifying the gene product which is underexpressed in a strain which proliferated more slowly in said culture.

399. The method of Paragraph 393, 394, 395, 396, 397 or 398, wherein at least one strain in said culture does not underexpresses a gene product which is essential for proliferation of said organism.

400. The method of Paragraph 393, 394, 395, 396, 397 or 398, wherein said strains which underexpress said gene products comprise a nucleic acid complementary to at least a portion of a gene encoding said gene product which is essential for proliferation of said organism operably linked to a regulatable promoter.

401. The method of Paragraph 393, 394, 395, 396, 397 or 398, wherein said strains which underexpress said gene products express an antisense nucleic acid complementary to at least

a portion of a gene encoding said gene product which is essential for proliferation of said organism, wherein expression of said antisense nucleic acid reduces expression of said gene product in said strain.

402. The method of Paragraph 393, 394, 395, 396, 397 or 398, wherein said  
5 identification step comprises determining the nucleotide sequence of a nucleic acid encoding said gene product in said strain which proliferated more slowly.

403. The method of Paragraph 393, 394, 395, 396, 397 or 398, wherein said identification step comprises performing an amplification reaction to identify the nucleic acid encoding said gene product in said cell which proliferated more slowly.

10 404. The method of Paragraph 393, 394, 395, 396, 397 or 398, wherein the products of said amplification reaction are labeled with a detectable dye.

405. The method of Paragraph 404, wherein said identification step comprises performing a hybridization procedure.

406. The method of Paragraph 393, 394, 395, 396, 397 or 398, wherein said  
15 identification step comprises contacting a nucleic acid array with a nucleic acid encoding said gene product in said cell which proliferated more slowly.

407. The method of Paragraph 393, 394, 395, 396, 397 or 398, wherein said organism is selected from the group consisting of bacteria, fungi, protozoa.

408. The method of Paragraph 393, 394, 395, 396, 397 or 398, wherein said culture is a  
20 culture of an organism selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr*  
25 (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*,  
30 *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*,  
35 *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*,

*Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

409. The method of Paragraph 393, 394, 395, 396, 397 or 398, wherein said compound is obtained from a library of natural compounds.

5 410. The method of Paragraph 393, 394, 395, 396, 397 or 398, wherein said compound is obtained from a library of synthetic compounds.

411. The method of Paragraph 393, 394, 395, 396, 397 or 398, wherein said compound is present in a crude or partially purified state.

412. The method of Paragraph 393, 394, 395, 396, 397 or 398, further comprising  
10 determining whether said gene product in said strain which proliferated more slowly in said culture has a counterpart in at least one other organism.

413. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

obtaining a plurality of cultures, each culture comprising a plurality of strains  
15 wherein each strain underexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product whose activity or level is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 is underexpressed;

contacting each of said cultures with a different concentration of said compound;  
20 and

identifying the gene product which is underexpressed in a strain whose rate of proliferation is reduced by said compound.

414. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

25 obtaining a plurality of cultures, each culture comprising a plurality of strains wherein each strain underexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 6214-42397 is underexpressed;

30 contacting each of said cultures with a different concentration of said compound; and

identifying the gene product which is underexpressed in a strain whose rate of proliferation is reduced by said compound.

415. A method for identifying the gene product on which a compound which inhibits  
35 proliferation of an organism acts comprising:

obtaining a plurality of cultures, each culture comprising a plurality of strains wherein each strain underexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene

product comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42938-78581 is underexpressed;

contacting each of said cultures with a different concentration of said compound;

and

5 identifying the gene product which is underexpressed in a strain whose rate of proliferation is reduced by said compound.

416. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

obtaining a plurality of cultures, each culture comprising a plurality of strains  
10 wherein each strain underexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product selected from the group consisting of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a  
15 nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product having at least 25% amino acid identity as determined using FASTA  
20 version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 under stringent conditions, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group  
25 consisting of SEQ ID NOs.: 1-6213 is underexpressed;

contacting each of said cultures with a different concentration of said compound;

and

identifying the gene product which is underexpressed in a strain whose rate of proliferation is reduced by said compound.

35 417. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

obtaining a plurality of cultures, each culture comprising a plurality of strains wherein each strain underexpresses a different gene product which is essential for

proliferation of said organism, wherein said culture comprises a strain in which a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of a nucleic acid comprising a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397, a nucleic acid comprising a nucleotide sequence which hybridizes to a sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under stringent conditions, and a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under moderate conditions is underexpressed;

contacting each of said cultures with a different concentration of said compound;  
and

identifying the gene product which is underexpressed in a strain whose rate of proliferation is reduced by said compound.

418. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

obtaining a plurality of cultures, each culture comprising a plurality of strains wherein each strain underexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product comprises a polypeptide selected from the group consisting of a polypeptide having at least 25% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide selected from the group consisting of SEQ ID NOS.: 42938-78581 and a polypeptide whose activity may be complemented by a polypeptide selected from the group consisting of SEQ ID NOS: 42938-78581 is underexpressed;

contacting each of said cultures with a different concentration of said compound;  
and

identifying the gene product which is underexpressed in a strain whose rate of proliferation is reduced by said compound.

419. A method of profiling a compound's activity comprising:

performing the method of Paragraph 393 on a first culture using a first compound;  
performing the method of Paragraph 393 on a second culture using a second compound; and

comparing the strains identified in said first culture to the strains identified in said second culture.

420. A method of profiling a compound's activity comprising:

performing the method of Paragraph 394 on a first culture using a first compound;  
performing the method of Paragraph 394 on a second culture using a second compound; and

comparing the strains identified in said first culture to the strains identified in said second culture.

421. A method of profiling a compound's activity comprising:

performing the method of Paragraph 395 on a first culture using a first compound;

performing the method of Paragraph 395 on a second culture using a second compound; and

comparing the strains identified in said first culture to the strains identified in said second culture.

422. A method of profiling a compound's activity comprising

performing the method of Paragraph 396 on a first culture using a first compound;

performing the method of Paragraph 396 on a second culture using a second compound; and

comparing the strains identified in said first culture to the strains identified in said second culture.

423. A method of profiling a compound's activity comprising

performing the method of Paragraph 397 on a first culture using a first compound;

performing the method of Paragraph 397 on a second culture using a second compound; and

comparing the strains identified in said first culture to the strains identified in said second culture.

424. A method of profiling a compound's activity comprising

performing the method of Paragraph 398 on a first culture using a first compound;

performing the method of Paragraph 398 on a second culture using a second compound; and

comparing the strains identified in said first culture to the strains identified in said second culture.

425. A method of profiling a first compound's activity comprising:

growing an array of strains on a first solid medium comprising said first compound and on a second solid medium comprising a second compound, wherein said array comprises a plurality of strains wherein each strain underexpresses a different gene product which is essential for proliferation of an organism, wherein said culture comprises a strain in which a gene product whose activity or level is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 is underexpressed, and wherein said first compound and said second compound inhibit the proliferation of said organism; and

comparing the pattern of strains which grow on said first solid medium with the pattern of strains which grow on said second solid medium.

426. A method of profiling a first compound's activity comprising:



growing an array of strains on a first solid medium comprising said first compound and on a second solid medium comprising a second compound, wherein said array comprises a plurality of strains wherein each strain underexpresses a different gene product which is essential for proliferation of an organism, wherein said culture comprises a strain in which a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 6214-42397 is underexpressed, and wherein said first compound and said second compound inhibit the proliferation of said organism; and

comparing the pattern of strains which grow on said first solid medium with the pattern of strains which grow on said second solid medium.

427. A method of profiling a first compound's activity comprising:

growing an array of strains on a first solid medium comprising said first compound and on a second solid medium comprising a second compound, wherein said array comprises a plurality of strains wherein each strain underexpresses a different gene product which is essential for proliferation of an organism, wherein said culture comprises a strain in which a gene product comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42938-78581 is underexpressed, and wherein said first compound and said second compound inhibit the proliferation of said organism; and

comparing the pattern of strains which grow on said first solid medium with the pattern of strains which grow on said second solid medium.

428. A method of profiling a first compound's activity comprising:

growing an array of strains on a first solid medium comprising said first compound and on a second solid medium comprising a second compound, wherein said array comprises a plurality of strains wherein each strain underexpresses a different gene product which is essential for proliferation of an organism, wherein said culture comprises a strain in which a gene product selected from the group consisting of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group

consisting of SEQ ID NOS.: 1-6213 under stringent conditions, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 1-6213 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 1-6213 is underexpressed, and wherein said first compound and said second compound inhibit the proliferation of said organism; and

comparing the pattern of strains which grow on said first solid medium with the pattern of strains which grow on said second solid medium.

429. A method of profiling a first compound's activity comprising:

growing an array of strains on a first solid medium comprising said first compound and on a second solid medium comprising a second compound, wherein said array comprises a plurality of strains wherein each strain underexpresses a different gene product which is essential for proliferation of an organism, wherein said culture comprises a strain in which a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of a nucleic acid comprising a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397, a nucleic acid comprising a nucleotide sequence which hybridizes to a sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under stringent conditions, and a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under moderate conditions is underexpressed, and wherein said first compound and said second compound inhibit the proliferation of said organism; and

comparing the pattern of strains which grow on said first solid medium with the pattern of strains which grow on said second solid medium.

430. A method of profiling a first compound's activity comprising:

growing an array of strains on a first solid medium comprising said first compound and on a second solid medium comprising a second compound, wherein said array comprises a plurality of strains wherein each strain underexpresses a different gene product which is essential for proliferation of an organism, wherein said culture comprises a strain in which a gene product comprises a polypeptide selected from the group consisting of a polypeptide having at least 25% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide selected from the group consisting of SEQ ID NOS.: 42938-78581 and a polypeptide whose activity may be complemented by a polypeptide selected from the group consisting of SEQ ID NOS.: 42938-78581 is underexpressed, and wherein said first compound and said second compound inhibit the proliferation of said organism; and

comparing the pattern of strains which grow on said first solid medium with the pattern of strains which grow on said second solid medium.

431. The method of any one of Paragraphs 419, 420, 421, 422, 423, 424, 425, 426, 427, 428, 429 or 430, wherein said first compound is present in a crude or partially purified state.

5 432. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

obtaining a plurality of cultures comprising a plurality of strains wherein each strain underexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product whose activity or level is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 is underexpressed;

contacting each of said plurality of cultures with a varying concentration of a regulatory agent which regulates the level of expression of said gene products which are essential for proliferation of said organism; and

15 identifying the gene product which is underexpressed in a strain whose rate of proliferation is reduced by said compound.

433. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

20 obtaining a plurality of cultures comprising a plurality of strains wherein each strain underexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 6214-42397 is underexpressed;

25 contacting each of said plurality of cultures with a varying concentration of a regulatory agent which regulates the level of expression of said gene products which are essential for proliferation of said organism; and

identifying the gene product which is underexpressed in a strain whose rate of proliferation is reduced by said compound.

30 434. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

35 obtaining a plurality of cultures comprising a plurality of strains wherein each strain underexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42938-78581 is underexpressed;

contacting each of said plurality of cultures with a varying concentration of a regulatory agent which regulates the level of expression of said gene products which are essential for proliferation of said organism; and

identifying the gene product which is underexpressed in a strain whose rate of proliferation is reduced by said compound.

435. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

5 obtaining a plurality of cultures comprising a plurality of strains wherein each strain underexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product selected from the group consisting of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product  
10 whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide  
15 sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 under stringent conditions, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 is underexpressed;

contacting each of said plurality of cultures with a varying concentration of a regulatory agent which regulates the level of expression of said gene products which are essential for proliferation of said organism; and

30 identifying the gene product which is underexpressed in a strain whose rate of proliferation is reduced by said compound.

436. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

35 obtaining a plurality of cultures comprising a plurality of strains wherein each strain underexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of a nucleic acid comprising a nucleic acid having at least 70% nucleotide sequence identity as

determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397, a nucleic acid comprising a nucleotide sequence which hybridizes to a sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under stringent conditions, and a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under moderate conditions is underexpressed;

contacting each of said plurality of cultures with a varying concentration of a regulatory agent which regulates the level of expression of said gene products which are essential for proliferation of said organism; and

identifying the gene product which is underexpressed in a strain whose rate of proliferation is reduced by said compound.

437. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

obtaining a plurality of cultures comprising a plurality of strains wherein each strain underexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product comprises a polypeptide selected from the group consisting of a polypeptide having at least 25% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide selected from the group consisting of SEQ ID NOS.: 42938-78581 and a polypeptide whose activity may be complemented by a polypeptide selected from the group consisting of SEQ ID NOS: 42938-78581 is underexpressed;

contacting each of said plurality of cultures with a varying concentration of a regulatory agent which regulates the level of expression of said gene products which are essential for proliferation of said organism; and

identifying the gene product which is underexpressed in a strain whose rate of proliferation is reduced by said compound.

438. A culture comprising a plurality of strains wherein each strain overexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product whose activity or level is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 1-6213 is overexpressed.

439. A culture comprising a plurality of strains wherein each strain overexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 is overexpressed.

440. A culture comprising a plurality of strains wherein each strain overexpresses a different gene product which is essential for proliferation of said organism, wherein said culture

comprises a strain in which a gene product comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42938-78581 is overexpressed.

441. A culture comprising a plurality of strains wherein each strain overexpresses a different gene product which is essential for proliferation of said organism, wherein said culture  
5 comprises a strain in which a gene product selected from the group consisting of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a  
10 gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide  
15 sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 under stringent conditions, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 under moderate conditions, and a gene product whose  
20 activity may be complemented by the gene product whose activity is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 is overexpressed.

442. A culture comprising a plurality of strains wherein each strain overexpresses a different gene product which is essential for proliferation of said organism, wherein said culture  
25 comprises a strain in which a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of a nucleic acid comprising a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397, a nucleic acid comprising a nucleotide sequence which hybridizes to a sequence selected  
30 from the group consisting of SEQ ID NOS.: 6214-42397 under stringent conditions, and a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under moderate conditions is overexpressed.

443. A culture comprising a plurality of strains wherein each strain overexpresses a different gene product which is essential for proliferation of said organism, wherein said culture  
35 comprises a strain in which a gene product comprises a polypeptide selected from the group consisting of a polypeptide having at least 25% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide selected from the group consisting of SEQ ID NOs.: 42938-78581

and a polypeptide whose activity may be complemented by a polypeptide selected from the group consisting of SEQ ID NOs: 42938-78581 is overexpressed.

444. The culture of Paragraph 438, 439, 440, 441, 442 or 443, wherein said strains which overexpress said gene products comprise a nucleic acid encoding said gene product which is essential for proliferation of said organism operably linked to a regulatable promoter.

445. The culture of Paragraph 438, 439, 440, 441, 442 or 443, wherein said strains which overexpress said gene products comprise a nucleic acid encoding said gene product which is essential for proliferation of said organism operably linked to a constitutive promoter.

446. The culture of Paragraph 438, 439, 440, 441, 442 or 443, wherein said culture is a culture of an organism selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

447. A culture comprising a plurality of strains wherein each strain underexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product whose activity or level is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 is underexpressed.

448. A culture comprising a plurality of strains wherein each strain underexpresses a different gene product which is essential for proliferation of said organism, wherein said culture

comprises a strain in which a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 6214-42397 is underexpressed.

449. A culture comprising a plurality of strains wherein each strain underexpresses a different gene product which is essential for proliferation of said organism, wherein said culture  
5 comprises a strain in which a gene product comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42938-78581 is underexpressed.

450. A culture comprising a plurality of strains wherein each strain underexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product selected from the group consisting of a gene product  
10 having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a  
15 gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a  
20 nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 under stringent conditions, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid  
25 comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 is underexpressed.

451. A culture comprising a plurality of strains wherein each strain underexpresses a different gene product which is essential for proliferation of said organism, wherein said culture comprises a strain in which a gene product encoded by a nucleic acid comprising a nucleotide  
30 sequence selected from the group consisting of a nucleic acid comprising a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397, a nucleic acid comprising a nucleotide sequence which hybridizes to a sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under stringent conditions, and a nucleic  
35 acid comprising a nucleotide sequence which hybridizes to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under moderate conditions is underexpressed.

452. A culture comprising a plurality of strains wherein each strain underexpresses a different gene product which is essential for proliferation of said organism, wherein said culture



comprises a strain in which a gene product comprises a polypeptide selected from the group consisting of a polypeptide having at least 25% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide selected from the group consisting of SEQ ID NOs.: 42938-78581 and a polypeptide whose activity may be complemented by a polypeptide selected from the group consisting of SEQ ID NOs: 42938-78581 is underexpressed.

453. The culture of Paragraph 447, 448, 449, 450, 451 or 452, wherein said strains which underexpress said gene products comprise a nucleic acid encoding said gene product which is essential for proliferation of said organism operably linked to a regulatable promoter.

454. The culture of Paragraph 447, 448, 449, 450, 451 or 452, wherein said strains which underexpress said gene products comprise a nucleic acid encoding said gene product which is essential for proliferation of said organism operably linked to a constitutive promoter.

455. The culture of Paragraph 447, 448, 449, 450, 451 or 452, wherein said culture is a culture of an organism selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

456. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

obtaining a culture comprising a plurality of strains wherein each strain overexpresses a different gene product which is essential for proliferation of said organism and wherein the nucleotide sequence of each of the overexpressed genes has been altered so

as to include a nucleotide sequence which can be used to generate a unique product corresponding to each of the overexpressed genes, wherein said culture comprises a strain in which a gene product whose activity or level is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 is overexpressed;

contacting said culture with a sufficient concentration of said compound to inhibit the proliferation of strains of said organism which do not overexpress said gene product on which said compound acts, such that strains which overexpress said gene product on which said compound acts proliferate more rapidly than strains which do not overexpress said gene product on which said compound acts; and

identifying the gene product which is overexpressed in a strain which proliferated more rapidly in said culture by detecting the unique product corresponding to said gene.

457. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

obtaining a culture comprising a plurality of strains wherein each strain overexpresses a different gene product which is essential for proliferation of said organism and wherein the nucleotide sequence of each of the overexpressed genes has been altered so as to include a nucleotide sequence which can be used to generate a unique product corresponding to each of the overexpressed genes, wherein said culture comprises a strain in which a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 6214-42397 is overexpressed;

contacting said culture with a sufficient concentration of said compound to inhibit the proliferation of strains of said organism which do not overexpress said gene product on which said compound acts, such that strains which overexpress said gene product on which said compound acts proliferate more rapidly than strains which do not overexpress said gene product on which said compound acts; and

identifying the gene product which is overexpressed in a strain which proliferated more rapidly in said culture by detecting the unique product corresponding to said gene.

458. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

obtaining a culture comprising a plurality of strains wherein each strain overexpresses a different gene product which is essential for proliferation of said organism and wherein the nucleotide sequence of each of the overexpressed genes has been altered so as to include a nucleotide sequence which can be used to generate a unique product corresponding to each of the overexpressed genes, wherein said culture comprises a strain in which a gene product comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42938-78581 is overexpressed;

contacting said culture with a sufficient concentration of said compound to inhibit the proliferation of strains of said organism which do not overexpress said gene product on which said compound acts, such that strains which overexpress said gene product on which said compound acts proliferate more rapidly than strains which do not overexpress said gene product on which said compound acts; and

identifying the gene product which is overexpressed in a strain which proliferated more rapidly in said culture by detecting the unique product corresponding to said gene.

459. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

obtaining a culture comprising a plurality of strains wherein each strain overexpresses a different gene product which is essential for proliferation of said organism and wherein the nucleotide sequence of each of the overexpressed genes has been altered so as to include a nucleotide sequence which can be used to generate a unique product corresponding to each of the overexpressed genes, wherein said culture comprises a strain in which a gene product selected from the group consisting of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 under stringent conditions, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 is overexpressed;

contacting said culture with a sufficient concentration of said compound to inhibit the proliferation of strains of said organism which do not overexpress said gene product on which said compound acts, such that strains which overexpress said gene product on which said compound acts proliferate more rapidly than strains which do not overexpress said gene product on which said compound acts; and

identifying the gene product which is overexpressed in a strain which proliferated more rapidly in said culture by detecting the unique product corresponding to said gene.

460. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

5 obtaining a culture comprising a plurality of strains wherein each strain overexpresses a different gene product which is essential for proliferation of said organism and wherein the nucleotide sequence of each of the overexpressed genes has been altered so as to include a nucleotide sequence which can be used to generate a unique product corresponding to each of the overexpressed genes, wherein said culture comprises a strain  
10 in which a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of a nucleic acid comprising a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397, a nucleic acid comprising a nucleotide sequence which hybridizes to a  
15 sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under stringent conditions, and a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under moderate conditions is overexpressed;

contacting said culture with a sufficient concentration of said compound to inhibit  
20 the proliferation of strains of said organism which do not overexpress said gene product on which said compound acts, such that strains which overexpress said gene product on which said compound acts proliferate more rapidly than strains which do not overexpress said gene product on which said compound acts; and

identifying the gene product which is overexpressed in a strain which proliferated  
25 more rapidly in said culture by detecting the unique product corresponding to said gene.

461. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

obtaining a culture comprising a plurality of strains wherein each strain  
30 overexpresses a different gene product which is essential for proliferation of said organism and wherein the nucleotide sequence of each of the overexpressed genes has been altered so as to include a nucleotide sequence which can be used to generate a unique product corresponding to each of the overexpressed genes, wherein said culture comprises a strain in which a gene product comprises a polypeptide selected from the group consisting of a polypeptide having at least 25% amino acid identity as determined using FASTA version  
35 3.0t78 to a polypeptide selected from the group consisting of SEQ ID NOs.: 42938-78581 and a polypeptide whose activity may be complemented by a polypeptide selected from the group consisting of SEQ ID NOs: 42938-78581 is overexpressed;

contacting said culture with a sufficient concentration of said compound to inhibit the proliferation of strains of said organism which do not overexpress said gene product on which said compound acts, such that strains which overexpress said gene product on which said compound acts proliferate more rapidly than strains which do not overexpress said gene product on which said compound acts; and

identifying the gene product which is overexpressed in a strain which proliferated more rapidly in said culture by detecting the unique product corresponding to said gene.

462. The method of Paragraph 456, 457, 458, 459, 460 or 461, wherein the nucleotide sequence of each of the genes encoding an overexpressed gene product has been altered by replacing the native promoters of said genes with promoters which facilitate overexpression of said gene products.

463. The method of Paragraph 456, 457, 458, 459, 460 or 461, wherein the nucleotide sequence of each of the genes encoding an overexpressed gene product has been altered by inserting a regulatory element into the native promoters of said genes with a promoter which facilitates overexpression of said gene products.

464. The method of Paragraph 463, wherein said regulatory element is selected from the group consisting of a regulatable promoter, an operator which is recognized by a repressor, a nucleotide sequence which is recognized by a transcriptional activator, a transcriptional terminator, a nucleotide sequence which introduces a bend in the DNA and an upstream activating sequence.

465. The method of Paragraph 456, 457, 458, 459, 460 or 461, wherein the step of identifying the gene product which is overexpressed in a strain which proliferated more rapidly in said culture by detecting the unique product corresponding to said gene comprises performing an amplification reaction and detecting a unique amplification product corresponding to said gene.

466. The method of Paragraph 462, wherein the native promoter of each of the genes encoding a gene product essential for proliferation is replaced with the same promoter.

467. The method of Paragraph 462, wherein the native promoters of the genes encoding gene products essential for proliferation are replaced with a plurality of promoters selected to give a desired expression level for each gene product.

468. The method of Paragraph 462, wherein said promoters which replaced the native promoters in each strain comprise regulatable promoters.

469. The method of Paragraph 462, wherein said promoters which replaced the native promoters in each strain each strain comprise constitutive promoters.

470. The method of Paragraph 456, 457, 458, 459, 460 or 461, wherein said organism is selected from the group consisting of bacteria, fungi, and protozoa.

471. The method of Paragraph 456, 457, 458, 459, 460 or 461, wherein said culture is a culture of an organism selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*,

*Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium*  
 5 *perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma*  
 10 *genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*,  
 15 *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

472. A method for identifying the gene product on which a compound which inhibits  
 20 proliferation of an organism acts comprising:

obtaining a culture comprising a plurality of strains wherein each strain underexpresses a different gene product which is essential for proliferation of said organism and wherein the nucleotide sequence of each of the underexpressed genes has been altered so as to include a nucleotide sequence which can be used to generate a unique product  
 25 corresponding to each of the underexpressed genes and wherein said culture comprises a strain in which a gene product whose activity or level is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 is underexpressed;

contacting said culture with a sufficient concentration of said compound to inhibit  
 30 the proliferation of strains of said organism which underexpress said gene product on which said compound acts, such that strains which underexpress said gene product on which said compound acts proliferate more slowly than strains which do not underexpress the gene product on which said compound acts; and

identifying the gene product which is underexpressed in a strain which proliferated  
 35 more rapidly in said culture by detecting the unique product corresponding to said gene.

473. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

obtaining a culture comprising a plurality of strains wherein each strain underexpresses a different gene product which is essential for proliferation of said organism and wherein the nucleotide sequence of each of the underexpressed genes has been altered so as to include a nucleotide sequence which can be used to generate a unique product corresponding to each of the underexpressed genes and wherein said culture comprises a strain in which a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 6214-42397 is underexpressed;

contacting said culture with a sufficient concentration of said compound to inhibit the proliferation of strains of said organism which underexpress said gene product on which said compound acts, such that strains which underexpress said gene product on which said compound acts proliferate more slowly than strains which do not underexpress the gene product on which said compound acts; and

identifying the gene product which is underexpressed in a strain which proliferated more rapidly in said culture by detecting the unique product corresponding to said gene.

474. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

obtaining a culture comprising a plurality of strains wherein each strain underexpresses a different gene product which is essential for proliferation of said organism and wherein the nucleotide sequence of each of the underexpressed genes has been altered so as to include a nucleotide sequence which can be used to generate a unique product corresponding to each of the underexpressed genes, wherein said culture comprises a strain in which a gene product comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42938-78581 is underexpressed;

contacting said culture with a sufficient concentration of said compound to inhibit the proliferation of strains of said organism which underexpress said gene product on which said compound acts, such that strains which underexpress said gene product on which said compound acts proliferate more slowly than strains which do not underexpress the gene product on which said compound acts; and

identifying the gene product which is underexpressed in a strain which proliferated more rapidly in said culture by detecting the unique product corresponding to said gene.

475. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

obtaining a culture comprising a plurality of strains wherein each strain underexpresses a different gene product which is essential for proliferation of said organism and wherein the nucleotide sequence of each of the underexpressed genes has been altered so as to include a nucleotide sequence which can be used to generate a unique product corresponding to each of the underexpressed genes, wherein said culture comprises a strain in which a gene product selected from the group consisting of a gene product having at

least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 under stringent conditions, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 is underexpressed;

contacting said culture with a sufficient concentration of said compound to inhibit the proliferation of strains of said organism which underexpress said gene product on which said compound acts, such that strains which underexpress said gene product on which said compound acts proliferate more slowly than strains which do not underexpress the gene product on which said compound acts; and

identifying the gene product which is underexpressed in a strain which proliferated more rapidly in said culture by detecting the unique product corresponding to said gene.

476. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

obtaining a culture comprising a plurality of strains wherein each strain underexpresses a different gene product which is essential for proliferation of said organism and wherein the nucleotide sequence of each of the underexpressed genes has been altered so as to include a nucleotide sequence which can be used to generate a unique product corresponding to each of the underexpressed genes, wherein said culture comprises a strain in which a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of a nucleic acid comprising a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397, a nucleic acid comprising a nucleotide sequence which hybridizes to a sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under stringent



conditions, and a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under moderate conditions is underexpressed;

5           contacting said culture with a sufficient concentration of said compound to inhibit the proliferation of strains of said organism which underexpress said gene product on which said compound acts, such that strains which underexpress said gene product on which said compound acts proliferate more slowly than strains which do not underexpress the gene product on which said compound acts; and

10           identifying the gene product which is underexpressed in a strain which proliferated more rapidly in said culture by detecting the unique product corresponding to said gene.

477. A method for identifying the gene product on which a compound which inhibits proliferation of an organism acts comprising:

15           obtaining a culture comprising a plurality of strains wherein each strain underexpresses a different gene product which is essential for proliferation of said organism and wherein the nucleotide sequence of each of the underexpressed genes has been altered so as to include a nucleotide sequence which can be used to generate a unique product corresponding to each of the underexpressed genes, wherein said culture comprises a strain in which a gene product comprises a polypeptide selected from the group consisting of a polypeptide having at least 25% amino acid identity as determined using FASTA version 20 3.0t78 to a polypeptide selected from the group consisting of SEQ ID NOS.: 42938-78581 and a polypeptide whose activity may be complemented by a polypeptide selected from the group consisting of SEQ ID NOS: 42938-78581 is underexpressed;

25           contacting said culture with a sufficient concentration of said compound to inhibit the proliferation of strains of said organism which underexpress said gene product on which said compound acts, such that strains which underexpress said gene product on which said compound acts proliferate more slowly than strains which do not underexpress the gene product on which said compound acts; and

30           identifying the gene product which is underexpressed in a strain which proliferated more rapidly in said culture by detecting the unique product corresponding to said gene.

478. The method of Paragraph 472, 473, 474, 475, 476 or 477, wherein the nucleotide sequence of each of the genes encoding an underexpressed gene product has been altered by replacing the native promoters of said genes with promoters which facilitate underexpression of said gene products.

35           479. The method of Paragraph 472, 473, 474, 475, 476 or 477, wherein the nucleotide sequence of each of the genes encoding an underexpressed gene product has been altered by inserting a regulatory element into the native promoters of said genes with a promoter which facilitates underexpression of said gene products.

480. The method of Paragraph 479, wherein said regulatory element is selected from the group consisting of a regulatable promoter, an operator which is recognized by a repressor, a nucleotide sequence which is recognized by a transcriptional activator, a transcriptional terminator, a nucleotide sequence which introduces a bend in the DNA and an upstream activating sequence.

5 481. The method of Paragraph 472, 473, 474, 475, 476 or 477, wherein the step of identifying the gene product which is underexpressed in a strain which proliferated more slowly in said culture by detecting the unique product corresponding to said gene comprises performing an amplification reaction and detecting a unique amplification product corresponding to said gene.

482. The method of Paragraph 478, wherein the native promoter of each of the genes  
10 encoding a gene product essential for proliferation is replaced with the same promoter.

483. The method of Paragraph 478, wherein the native promoters of the genes encoding gene products essential for proliferation are replaced with a plurality of promoters selected to give a desired expression level for each gene product.

484. The method of Paragraph 478, wherein said promoters which replaced the native  
15 promoters in each strain comprise regulatable promoters.

485. The method of Paragraph 478, wherein said promoters which replaced the native promoters in each strain each strain comprise constitutive promoters.

486. The method of Paragraph 472, 473, 474, 475, 476 or 477, wherein said organism is selected from the group consisting of bacteria, fungi, and protozoa.

20 487. The method of Paragraph 472, 473, 474, 475, 476 or 477, wherein said culture is a culture of an organism selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*),  
25 *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*,  
30 *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*,

*Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* and any species falling within the genera of any of the above species.

488. A method for determining the extent to which each of a plurality of strains are  
5 present in a culture or collection of strains comprising:

obtaining a nucleic acid sample comprising nucleic acids from a culture or  
collection of strains wherein said culture or collection of strains comprises a plurality of  
strains wherein each strain overexpresses or underexpresses a different gene product which  
is required for proliferation of said organism wherein said culture comprises a strain in  
10 which a gene product whose activity or level is inhibited by a nucleic acid comprising a  
nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 is  
overexpressed or underexpressed;

performing an amplification reaction using a set of primer pairs which are  
complementary to nucleotide sequences within or adjacent to the genes which encode said  
15 gene products, wherein the members of said set of primer pairs are designed such that each  
primer pair would yield an amplification product having a length distinguishable from the  
lengths of the amplification products from the other primer pairs if a strain comprising the  
nucleotide sequences complementary to said primer pair is present in said culture or  
collection of strains; and

20 determining the lengths of the amplification products obtained in said amplification  
reaction.

489. A method for determining the extent to which each of a plurality of strains are  
present in a culture or collection of strains comprising:

obtaining a nucleic acid sample comprising nucleic acids from a culture or  
25 collection of strains wherein said culture or collection of strains comprises a plurality of  
strains wherein each strain overexpresses or underexpresses a different gene product which  
is required for proliferation of said organism, wherein said culture comprises a strain in  
which a gene product encoded by a nucleic acid comprising a nucleotide sequence selected  
from the group consisting of SEQ ID NOs.: 6214-42397 is overexpressed or  
30 underexpressed;

performing an amplification reaction using a set of primer pairs which are  
complementary to nucleotide sequences within or adjacent to the genes which encode said  
gene products, wherein the members of said set of primer pairs are designed such that each  
primer pair would yield an amplification product having a length distinguishable from the  
35 lengths of the amplification products from the other primer pairs if a strain comprising the  
nucleotide sequences complementary to said primer pair is present in said culture or  
collection of strains; and

determining the lengths of the amplification products obtained in said amplification reaction.

490. A method for determining the extent to which each of a plurality of strains are present in a culture or collection of strains comprising:

5 obtaining a nucleic acid sample comprising nucleic acids from a culture or collection of strains wherein said culture or collection of strains comprises a plurality of strains wherein each strain overexpresses or underexpresses a different gene product which is required for proliferation of said organism, wherein said culture comprises a strain in which a gene product comprising an amino acid sequence selected from the group  
10 consisting of SEQ ID NOs.: 42938-78581 is overexpressed or underexpressed;

performing an amplification reaction using a set of primer pairs which are complementary to nucleotide sequences within or adjacent to the genes which encode said gene products, wherein the members of said set of primer pairs are designed such that each primer pair would yield an amplification product having a length distinguishable from the  
15 lengths of the amplification products from the other primer pairs if a strain comprising the nucleotide sequences complementary to said primer pair is present in said culture or collection of strains; and

determining the lengths of the amplification products obtained in said amplification reaction.

20 491. A method for determining the extent to which each of a plurality of strains are present in a culture or collection of strains comprising:

obtaining a nucleic acid sample comprising nucleic acids from a culture or collection of strains wherein said culture or collection of strains comprises a plurality of strains wherein each strain overexpresses or underexpresses a different gene product which  
25 is required for proliferation of said organism, wherein said culture comprises a strain in which a gene product selected from the group consisting of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.:  
30 1-6213, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product having at least 25% amino acid identity as determined using FASTA  
35 version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group

consisting of SEQ ID NOs.: 1-6213 under stringent conditions, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs: 1-6213 is overexpressed or underexpressed;

performing an amplification reaction using a set of primer pairs which are complementary to nucleotide sequences within or adjacent to the genes which encode said gene products, wherein the members of said set of primer pairs are designed such that each primer pair would yield an amplification product having a length distinguishable from the lengths of the amplification products from the other primer pairs if a strain comprising the nucleotide sequences complementary to said primer pair is present in said culture or collection of strains; and

determining the lengths of the amplification products obtained in said amplification reaction.

492. A method for determining the extent to which each of a plurality of strains are present in a culture or collection of strains comprising:

obtaining a nucleic acid sample comprising nucleic acids from a culture or collection of strains wherein said culture or collection of strains comprises a plurality of strains wherein each strain overexpresses or underexpresses a different gene product which is required for proliferation of said organism, wherein said culture comprises a strain in which a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of a nucleic acid comprising a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397, a nucleic acid comprising a nucleotide sequence which hybridizes to a sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under stringent conditions, and a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under moderate conditions is overexpressed or underexpressed;

performing an amplification reaction using a set of primer pairs which are complementary to nucleotide sequences within or adjacent to the genes which encode said gene products, wherein the members of said set of primer pairs are designed such that each primer pair would yield an amplification product having a length distinguishable from the lengths of the amplification products from the other primer pairs if a strain comprising the nucleotide sequences complementary to said primer pair is present in said culture or collection of strains; and

determining the lengths of the amplification products obtained in said amplification reaction.

493. A method for determining the extent to which each of a plurality of strains are present in a culture or collection of strains comprising:

5 obtaining a nucleic acid sample comprising nucleic acids from a culture or collection of strains wherein said culture or collection of strains comprises a plurality of strains wherein each strain overexpresses or underexpresses a different gene product which is required for proliferation of said organism, wherein said culture comprises a strain in which a gene product comprising a polypeptide selected from the group consisting of a  
10 polypeptide having at least 25% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide selected from the group consisting of SEQ ID NOs: 42938-78581 and a polypeptide whose activity may be complemented by a polypeptide selected from the group consisting of SEQ ID NOs: 42938-78581 is overexpressed or underexpressed;

performing an amplification reaction using a set of primer pairs which are  
15 complementary to nucleotide sequences within or adjacent to the genes which encode said gene products, wherein the members of said set of primer pairs are designed such that each primer pair would yield an amplification product having a length distinguishable from the lengths of the amplification products from the other primer pairs if a strain comprising the nucleotide sequences complementary to said primer pair is present in said culture or  
20 collection of strains; and

determining the lengths of the amplification products obtained in said amplification reaction.

494. The method of Paragraph 488, 489, 490, 491, 492 or 493, wherein one member of each primer pair for each of said genes is labeled with a detectable dye.

25 495. The method of Paragraph 488, 489, 490, 491, 492 or 493, wherein:

said nucleic acid sample is divided into N aliquots; and

said amplification reaction is performed on each aliquot using primer pairs complementary to nucleotide sequences within or adjacent to 1/N of the genes which encode said gene products, wherein one of the members of each primer pair in each aliquot  
30 is labeled with a dye and wherein the dyes on the primers in each aliquot are distinguishable from one another.

496. The method of Paragraph 494, further comprising pooling the amplification products from each of the aliquots prior to determining the lengths of the amplification products.

497. The method of Paragraph 488, 489, 490, 491, 492 or 493, wherein the native  
35 promoters of said genes which encode said gene products have been replaced with a regulatable promoter and one of the primers in said primer pairs is complementary to a nucleotide sequence within said regulatable promoter.

498. The method of Paragraph 496, wherein the native promoters for each of said genes were replaced with the same regulatable promoter.

499. The method of Paragraph 496, wherein more than one regulatable promoter was used to replace the promoters of said genes such that some of said genes are under the control of a  
5 different regulatable promoter.

500. A method for identifying the target of a compound which inhibits the proliferation of an organism comprising:

obtaining a first nucleic acid sample comprising nucleic acids from a first culture or collection of strains wherein said culture or collection of strains comprises a plurality of  
10 strains wherein each strain overexpresses or underexpresses a different gene product which is required for proliferation of said organism and wherein said culture or collection of strains has been contacted with said compound;

obtaining a second nucleic acid sample comprising nucleic acids from a second culture or collection of strains wherein said culture or collection of strains comprises the  
15 same strains as said first culture or collection of strains wherein said second culture or collection of strains has not been contacted with said compound;

performing a first amplification reaction on said first nucleic acid sample using a set of primer pairs which are complementary to nucleotide sequences within or adjacent to the genes which encode said gene products, wherein the members of said set of primer pairs  
20 are designed such that each primer pair would yield an amplification product having a length distinguishable from the lengths of the amplification products from the other primer pairs if a strain comprising the nucleotide sequences complementary to said primer pair is present in said culture or collection of strains;

performing a second amplification reaction on said second nucleic acid sample  
25 using the same set of primer pairs used in said first amplification reaction;

and comparing the amount of each amplification product in said first amplification reaction to the amount of that amplification product in said second amplification reaction, wherein an increased level of an amplification product in said first amplification reaction relative to said second amplification reaction indicates that the gene product corresponding  
30 to said amplification product is the target of said compound if said culture or strain overexpresses said gene products and a decreased level of of an amplification product in said first amplification reaction relative to said second amplification reaction indicates that the gene product corresponding to said amplification product is the target of said compound if said culture or strain overexpresses said gene products, wherein said first and second  
35 cultures or collection of strains comprise a strain in which a gene product whose activity or level is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 is overexpressed or underexpressed.

501. A method for identifying the target of a compound which inhibits the proliferation of an organism comprising:

obtaining a first nucleic acid sample comprising nucleic acids from a first culture or collection of strains wherein said culture or collection of strains comprises a plurality of strains wherein each strain overexpresses or underexpresses a different gene product which is required for proliferation of said organism and wherein said culture or collection of strains has been contacted with said compound;

obtaining a second nucleic acid sample comprising nucleic acids from a second culture or collection of strains wherein said culture or collection of strains comprises the same strains as said first culture or collection of strains wherein said second culture or collection of strains has not been contacted with said compound;

performing a first amplification reaction on said first nucleic acid sample using a set of primer pairs which are complementary to nucleotide sequences within or adjacent to the genes which encode said gene products, wherein the members of said set of primer pairs are designed such that each primer pair would yield an amplification product having a length distinguishable from the lengths of the amplification products from the other primer pairs if a strain comprising the nucleotide sequences complementary to said primer pair is present in said culture or collection of strains;

performing a second amplification reaction on said second nucleic acid sample using the same set of primer pairs used in said first amplification reaction;

and comparing the amount of each amplification product in said first amplification reaction to the amount of that amplification product in said second amplification reaction, wherein an increased level of an amplification product in said first amplification reaction relative to said second amplification reaction indicates that the gene product corresponding to said amplification product is the target of said compound if said culture or strain overexpresses said gene products and a decreased level of of an amplification product in said first amplification reaction relative to said second amplification reaction indicates that the gene product corresponding to said amplification product is the target of said compound if said culture or strain overexpresses said gene products, wherein said first and second cultures or collection of strains comprise a strain in which a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 6214-42397 is overexpressed or underexpressed.

502. A method for identifying the target of a compound which inhibits the proliferation of an organism comprising:

obtaining a first nucleic acid sample comprising nucleic acids from a first culture or collection of strains wherein said culture or collection of strains comprises a plurality of strains wherein each strain overexpresses or underexpresses a different gene product which



is required for proliferation of said organism and wherein said culture or collection of strains has been contacted with said compound;

obtaining a second nucleic acid sample comprising nucleic acids from a second culture or collection of strains wherein said culture or collection of strains comprises the same strains as said first culture or collection of strains wherein said second culture or collection of strains has not been contacted with said compound;

performing a first amplification reaction on said first nucleic acid sample using a set of primer pairs which are complementary to nucleotide sequences within or adjacent to the genes which encode said gene products, wherein the members of said set of primer pairs are designed such that each primer pair would yield an amplification product having a length distinguishable from the lengths of the amplification products from the other primer pairs if a strain comprising the nucleotide sequences complementary to said primer pair is present in said culture or collection of strains;

performing a second amplification reaction on said second nucleic acid sample using the same set of primer pairs used in said first amplification reaction;

and comparing the amount of each amplification product in said first amplification reaction to the amount of that amplification product in said second amplification reaction, wherein an increased level of an amplification product in said first amplification reaction relative to said second amplification reaction indicates that the gene product corresponding to said amplification product is the target of said compound if said culture or strain overexpresses said gene products and a decreased level of of an amplification product in said first amplification reaction relative to said second amplification reaction indicates that the gene product corresponding to said amplification product is the target of said compound if said culture or strain overexpresses said gene products, wherein said first and second cultures or collection of strains comprise a strain in which a gene product comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42938-78581 is overexpressed or underexpressed.

503. A method for identifying the target of a compound which inhibits the proliferation of an organism comprising:

obtaining a first nucleic acid sample comprising nucleic acids from a first culture or collection of strains wherein said culture or collection of strains comprises a plurality of strains wherein each strain overexpresses or underexpresses a different gene product which is required for proliferation of said organism and wherein said culture or collection of strains has been contacted with said compound;

obtaining a second nucleic acid sample comprising nucleic acids from a second culture or collection of strains wherein said culture or collection of strains comprises the same strains as said first culture or collection of strains wherein said second culture or collection of strains has not been contacted with said compound;

performing a first amplification reaction on said first nucleic acid sample using a set of primer pairs which are complementary to nucleotide sequences within or adjacent to the genes which encode said gene products, wherein the members of said set of primer pairs are designed such that each primer pair would yield an amplification product having a length distinguishable from the lengths of the amplification products from the other primer pairs if a strain comprising the nucleotide sequences complementary to said primer pair is present in said culture or collection of strains;

performing a second amplification reaction on said second nucleic acid sample using the same set of primer pairs used in said first amplification reaction;

and comparing the amount of each amplification product in said first amplification reaction to the amount of that amplification product in said second amplification reaction, wherein an increased level of an amplification product in said first amplification reaction relative to said second amplification reaction indicates that the gene product corresponding to said amplification product is the target of said compound if said culture or strain overexpresses said gene products and a decreased level of of an amplification product in said first amplification reaction relative to said second amplification reaction indicates that the gene product corresponding to said amplification product is the target of said compound if said culture or strain overexpresses said gene products, wherein said first and second cultures or collection of strains comprise a strain in which a gene product selected from the group consisting of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 under stringent conditions, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 is overexpressed or underexpressed.

504. A method for identifying the target of a compound which inhibits the proliferation of an organism comprising:

obtaining a first nucleic acid sample comprising nucleic acids from a first culture or collection of strains wherein said culture or collection of strains comprises a plurality of strains wherein each strain overexpresses or underexpresses a different gene product which is required for proliferation of said organism and wherein said culture or collection of strains has been contacted with said compound;

obtaining a second nucleic acid sample comprising nucleic acids from a second culture or collection of strains wherein said culture or collection of strains comprises the same strains as said first culture or collection of strains wherein said second culture or collection of strains has not been contacted with said compound;

performing a first amplification reaction on said first nucleic acid sample using a set of primer pairs which are complementary to nucleotide sequences within or adjacent to the genes which encode said gene products, wherein the members of said set of primer pairs are designed such that each primer pair would yield an amplification product having a length distinguishable from the lengths of the amplification products from the other primer pairs if a strain comprising the nucleotide sequences complementary to said primer pair is present in said culture or collection of strains;

performing a second amplification reaction on said second nucleic acid sample using the same set of primer pairs used in said first amplification reaction;

and comparing the amount of each amplification product in said first amplification reaction to the amount of that amplification product in said second amplification reaction, wherein an increased level of an amplification product in said first amplification reaction relative to said second amplification reaction indicates that the gene product corresponding to said amplification product is the target of said compound if said culture or strain overexpresses said gene products and a decreased level of of an amplification product in said first amplification reaction relative to said second amplification reaction indicates that the gene product corresponding to said amplification product is the target of said compound if said culture or strain overexpresses said gene products, wherein said first and second cultures or collection of strains comprise a strain in which a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of a nucleic acid comprising a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397, a nucleic acid comprising a nucleotide sequence which hybridizes to a sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under stringent conditions, and a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleotide sequence selected from

the group consisting of SEQ ID NOS.: 6214-42397 under moderate conditions is overexpressed or underexpressed.

505. A method for identifying the target of a compound which inhibits the proliferation of an organism comprising:

5 obtaining a first nucleic acid sample comprising nucleic acids from a first culture or collection of strains wherein said culture or collection of strains comprises a plurality of strains wherein each strain overexpresses or underexpresses a different gene product which is required for proliferation of said organism and wherein said culture or collection of strains has been contacted with said compound;

10 obtaining a second nucleic acid sample comprising nucleic acids from a second culture or collection of strains wherein said culture or collection of strains comprises the same strains as said first culture or collection of strains wherein said second culture or collection of strains has not been contacted with said compound;

15 performing a first amplification reaction on said first nucleic acid sample using a set of primer pairs which are complementary to nucleotide sequences within or adjacent to the genes which encode said gene products, wherein the members of said set of primer pairs are designed such that each primer pair would yield an amplification product having a length distinguishable from the lengths of the amplification products from the other primer pairs if a strain comprising the nucleotide sequences complementary to said primer pair is present in said culture or collection of strains;

20 performing a second amplification reaction on said second nucleic acid sample using the same set of primer pairs used in said first amplification reaction;

25 and comparing the amount of each amplification product in said first amplification reaction to the amount of that amplification product in said second amplification reaction, wherein an increased level of an amplification product in said first amplification reaction relative to said second amplification reaction indicates that the gene product corresponding to said amplification product is the target of said compound if said culture or strain overexpresses said gene products and a decreased level of of an amplification product in said first amplification reaction relative to said second amplification reaction indicates that  
30 the gene product corresponding to said amplification product is the target of said compound if said culture or strain overexpresses said gene products, wherein said first and second culture or collection of strains comprise a strain in which a gene product comprising a polypeptide selected from the group consisting of a polypeptide having at least 25% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide selected from the  
35 group consisting of SEQ ID NOS.: 42938-78581 and a polypeptide whose activity may be complemented by a polypeptide selected from the group consisting of SEQ ID NOS: 42938-78581 is overexpressed or underexpressed.

506. The method of Paragraph 500, 501, 502, 503, 504 or 505, wherein one member of each primer pair for each of said genes is labeled with a detectable dye.

507. The method of Paragraph 500, 501, 502, 503, 504 or 505, wherein the native promoters of said genes which encode said gene products have been replaced with a regulatable promoter and one of the primers in said primer pairs is complementary to a nucleotide sequence within said regulatable promoter.

508. The method of Paragraph 500, 501, 502, 503, 504 or 505, wherein the native promoters for each of said genes were replaced with the same regulatable promoter.

509. The method of Paragraph 500, 501, 502, 503, 504 or 505, wherein more than one regulatable promoter was used to replace the promoters of said genes such that some of said genes are under the control of a different regulatable promoter.

510. A method for determining the extent to which each of a plurality of strains are present in a culture or collection of strains comprising:

obtaining a nucleic acid sample comprising nucleic acids from a culture or collection of strains wherein said culture or collection of strains comprises a plurality of strains which transcribe an antisense nucleic acid complementary to a different gene product which is required for proliferation of said organism;

performing an amplification reaction using a set of primer pairs which are complementary to nucleotide sequences within or adjacent to the nucleic acids which encode said antisense nucleic acids, wherein the members of said set of primer pairs are designed such that each primer pair would yield an amplification product having a length distinguishable from the lengths of the amplification products from the other primer pairs if a strain comprising the nucleotide sequences complementary to said primer pair is present in said culture or collection of strains; and

determining the lengths of the amplification products obtained in said amplification reaction, wherein said culture comprises a strain in which a gene product whose activity or level is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 is overexpressed or underexpressed.

511. A method for determining the extent to which each of a plurality of strains are present in a culture or collection of strains comprising:

obtaining a nucleic acid sample comprising nucleic acids from a culture or collection of strains wherein said culture or collection of strains comprises a plurality of strains which transcribe an antisense nucleic acid complementary to a different gene product which is required for proliferation of said organism;

performing an amplification reaction using a set of primer pairs which are complementary to nucleotide sequences within or adjacent to the nucleic acids which encode said antisense nucleic acids, wherein the members of said set of primer pairs are designed such that each primer pair would yield an amplification product having a length

distinguishable from the lengths of the amplification products from the other primer pairs if a strain comprising the nucleotide sequences complementary to said primer pair is present in said culture or collection of strains; and

determining the lengths of the amplification products obtained in said amplification reaction, wherein said culture comprises a strain in which a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 6214-42397 is overexpressed or underexpressed.

512. A method for determining the extent to which each of a plurality of strains are present in a culture or collection of strains comprising:

obtaining a nucleic acid sample comprising nucleic acids from a culture or collection of strains wherein said culture or collection of strains comprises a plurality of strains which transcribe an antisense nucleic acid complementary to a different gene product which is required for proliferation of said organism;

performing an amplification reaction using a set of primer pairs which are complementary to nucleotide sequences within or adjacent to the nucleic acids which encode said antisense nucleic acids, wherein the members of said set of primer pairs are designed such that each primer pair would yield an amplification product having a length distinguishable from the lengths of the amplification products from the other primer pairs if a strain comprising the nucleotide sequences complementary to said primer pair is present in said culture or collection of strains; and

determining the lengths of the amplification products obtained in said amplification reaction, wherein said culture comprises a strain in which a gene product comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42938-78581 is overexpressed or underexpressed.

513. A method for determining the extent to which each of a plurality of strains are present in a culture or collection of strains comprising:

obtaining a nucleic acid sample comprising nucleic acids from a culture or collection of strains wherein said culture or collection of strains comprises a plurality of strains which transcribe an antisense nucleic acid complementary to a different gene product which is required for proliferation of said organism;

performing an amplification reaction using a set of primer pairs which are complementary to nucleotide sequences within or adjacent to the nucleic acids which encode said antisense nucleic acids, wherein the members of said set of primer pairs are designed such that each primer pair would yield an amplification product having a length distinguishable from the lengths of the amplification products from the other primer pairs if a strain comprising the nucleotide sequences complementary to said primer pair is present in said culture or collection of strains; and

determining the lengths of the amplification products obtained in said amplification reaction, wherein said culture comprises a strain in which a gene product selected from the group consisting of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 under stringent conditions, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 is overexpressed or underexpressed.

514. A method for determining the extent to which each of a plurality of strains are present in a culture or collection of strains comprising:

obtaining a nucleic acid sample comprising nucleic acids from a culture or collection of strains wherein said culture or collection of strains comprises a plurality of strains which transcribe an antisense nucleic acid complementary to a different gene product which is required for proliferation of said organism;

performing an amplification reaction using a set of primer pairs which are complementary to nucleotide sequences within or adjacent to the nucleic acids which encode said antisense nucleic acids, wherein the members of said set of primer pairs are designed such that each primer pair would yield an amplification product having a length distinguishable from the lengths of the amplification products from the other primer pairs if a strain comprising the nucleotide sequences complementary to said primer pair is present in said culture or collection of strains; and

determining the lengths of the amplification products obtained in said amplification reaction, wherein said culture comprises a strain in which a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of a nucleic acid comprising a nucleic acid having at least 70% nucleotide sequence identity as

determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397, a nucleic acid comprising a nucleotide sequence which hybridizes to a sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under stringent conditions, and a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under moderate conditions is overexpressed or underexpressed.

515. A method for determining the extent to which each of a plurality of strains are present in a culture or collection of strains comprising:

obtaining a nucleic acid sample comprising nucleic acids from a culture or collection of strains wherein said culture or collection of strains comprises a plurality of strains which transcribe an antisense nucleic acid complementary to a different gene product which is required for proliferation of said organism;

performing an amplification reaction using a set of primer pairs which are complementary to nucleotide sequences within or adjacent to the nucleic acids which encode said antisense nucleic acids, wherein the members of said set of primer pairs are designed such that each primer pair would yield an amplification product having a length distinguishable from the lengths of the amplification products from the other primer pairs if a strain comprising the nucleotide sequences complementary to said primer pair is present in said culture or collection of strains; and

determining the lengths of the amplification products obtained in said amplification reaction, wherein said culture comprises a strain in which a gene product comprising a polypeptide selected from the group consisting of a polypeptide having at least 25% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide selected from the group consisting of SEQ ID NOS.: 42938-78581 and a polypeptide whose activity may be complemented by a polypeptide selected from the group consisting of SEQ ID NOS.: 42938-78581 is overexpressed or underexpressed.

516. The method of Paragraph 510, 511, 512, 513, 514 or 515, wherein one member of each primer pair for each of said genes is labeled with a detectable dye.

517. The method of Paragraph 510, 511, 512, 513, 514 or 515, wherein:

said nucleic acid sample is divided into N aliquots; and

said amplification reaction is performed on each aliquot using primer pairs complementary to nucleotide sequences within or adjacent to 1/N of the genes which encode said gene products, wherein one of the members of each primer pair in each aliquot is labeled with a dye and wherein the dyes on the primers in each aliquot are distinguishable from one another.

518. The method of Paragraph 517, further comprising pooling the amplification products from each of the aliquots prior to determining the lengths of the amplification products.



519. A method for determining the extent to which each of a plurality of strains are present in a culture or collection of strains comprising:

obtaining a nucleic acid sample comprising nucleic acids from a culture or collection of strains wherein said culture or collection of strains comprises a plurality of strains which overexpress or underexpress a different gene product which is required for proliferation of said organism;

performing an amplification reaction using primer pairs which are complementary to nucleotide sequences within or adjacent to the genes which encode said gene products, wherein said primer pairs are designed such that each primer pair would yield an amplification product which is distinguishable from the amplification products produced by the other primer pairs on the a basis selected from the group consisting of length, detectable label and both length and detectable label if a strain comprising the nucleotide sequences complementary to said primer pair is present in said culture or collection of strains; and

identifying the amplification products obtained in said amplification reaction, wherein said culture comprises a strain in which a gene product whose activity or level is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 is overexpressed or underexpressed.

520. A method for determining the extent to which each of a plurality of strains are present in a culture or collection of strains comprising:

obtaining a nucleic acid sample comprising nucleic acids from a culture or collection of strains wherein said culture or collection of strains comprises a plurality of strains which overexpress or underexpress a different gene product which is required for proliferation of said organism;

performing an amplification reaction using primer pairs which are complementary to nucleotide sequences within or adjacent to the genes which encode said gene products, wherein said primer pairs are designed such that each primer pair would yield an amplification product which is distinguishable from the amplification products produced by the other primer pairs on the a basis selected from the group consisting of length, detectable label and both length and detectable label if a strain comprising the nucleotide sequences complementary to said primer pair is present in said culture or collection of strains; and

identifying the amplification products obtained in said amplification reaction, wherein said culture comprises a strain in which a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 6214-42397 is overexpressed or underexpressed.

521. A method for determining the extent to which each of a plurality of strains are present in a culture or collection of strains comprising:

obtaining a nucleic acid sample comprising nucleic acids from a culture or collection of strains wherein said culture or collection of strains comprises a plurality of

strains which overexpress or underexpress a different gene product which is required for proliferation of said organism;

performing an amplification reaction using primer pairs which are complementary to nucleotide sequences within or adjacent to the genes which encode said gene products, wherein said primer pairs are designed such that each primer pair would yield an amplification product which is distinguishable from the amplification products produced by the other primer pairs on the a basis selected from the group consisting of length, detectable label and both length and detectable label if a strain comprising the nucleotide sequences complementary to said primer pair is present in said culture or collection of strains; and

identifying the amplification products obtained in said amplification reaction, wherein said culture comprises a strain in which a gene product comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42938-78581 is overexpressed or underexpressed.

522. A method for determining the extent to which each of a plurality of strains are present in a culture or collection of strains comprising:

obtaining a nucleic acid sample comprising nucleic acids from a culture or collection of strains wherein said culture or collection of strains comprises a plurality of strains which overexpress or underexpress a different gene product which is required for proliferation of said organism;

performing an amplification reaction using primer pairs which are complementary to nucleotide sequences within or adjacent to the genes which encode said gene products, wherein said primer pairs are designed such that each primer pair would yield an amplification product which is distinguishable from the amplification products produced by the other primer pairs on the a basis selected from the group consisting of length, detectable label and both length and detectable label if a strain comprising the nucleotide sequences complementary to said primer pair is present in said culture or collection of strains; and

identifying the amplification products obtained in said amplification reaction, wherein said culture comprises a strain in which a gene product selected from the group consisting of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide

sequence selected from the group consisting of SEQ ID NOS.: 1-6213, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 1-6213 under stringent conditions, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 1-6213 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 1-6213 is overexpressed or underexpressed.

523. A method for determining the extent to which each of a plurality of strains are present in a culture or collection of strains comprising:

obtaining a nucleic acid sample comprising nucleic acids from a culture or collection of strains wherein said culture or collection of strains comprises a plurality of strains which overexpress or underexpress a different gene product which is required for proliferation of said organism;

performing an amplification reaction using primer pairs which are complementary to nucleotide sequences within or adjacent to the genes which encode said gene products, wherein said primer pairs are designed such that each primer pair would yield an amplification product which is distinguishable from the amplification products produced by the other primer pairs on the basis selected from the group consisting of length, detectable label and both length and detectable label if a strain comprising the nucleotide sequences complementary to said primer pair is present in said culture or collection of strains; and

identifying the amplification products obtained in said amplification reaction, wherein said culture comprises a strain in which a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of a nucleic acid comprising a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397, a nucleic acid comprising a nucleotide sequence which hybridizes to a sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under stringent conditions, and a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under moderate conditions is overexpressed or underexpressed.

524. A method for determining the extent to which each of a plurality of strains are present in a culture or collection of strains comprising:

obtaining a nucleic acid sample comprising nucleic acids from a culture or collection of strains wherein said culture or collection of strains comprises a plurality of

strains which overexpress or underexpress a different gene product which is required for proliferation of said organism;

performing an amplification reaction using primer pairs which are complementary to nucleotide sequences within or adjacent to the genes which encode said gene products, wherein said primer pairs are designed such that each primer pair would yield an amplification product which is distinguishable from the amplification products produced by the other primer pairs on the basis selected from the group consisting of length, detectable label and both length and detectable label if a strain comprising the nucleotide sequences complementary to said primer pair is present in said culture or collection of strains; and

identifying the amplification products obtained in said amplification reaction, wherein said culture comprises a strain in which a gene product comprising a polypeptide selected from the group consisting of a polypeptide having at least 25% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide selected from the group consisting of SEQ ID NOs.: 42938-78581 and a polypeptide whose activity may be complemented by a polypeptide selected from the group consisting of SEQ ID NOs: 42938-78581 is overexpressed or underexpressed.

525. The method of Paragraph 519, 520, 521, 522, 523 or 524, wherein said primer pairs are divided into at least two sets, each primer pair comprises a primer which is labeled with a distinguishable dye, and the distinguishable dye used to label each set of primer pairs is distinguishable from the dye used to label the other sets of primer pairs.

526. The method of Paragraph 519, 520, 521, 522, 523 or 524, wherein:

said nucleic acid sample is divided into N aliquots; and

said amplification reaction is performed on each aliquot using primer pairs complementary to nucleotide sequences within or adjacent to 1/N of the genes which encode said gene products, wherein one of the members of each primer pair in each aliquot is labeled with a dye and wherein the dyes on the primers in each aliquot are distinguishable from one another.

527. The method of Paragraph 526, further comprising pooling the amplification products from each of the aliquots prior to determining the lengths of the amplification products.

528. The method of Paragraph 519, 520, 521, 522, 523 or 524, wherein the native promoters of said genes which encode said gene products have been replaced with a regulatable promoter and one of the primers in said primer pairs is complementary to a nucleotide sequence within said regulatable promoter.

529. The method of Paragraph 528, wherein the native promoters for each of said genes were replaced with the same regulatable promoter.

530. The method of Paragraph 528, wherein more than one regulatable promoter was used to replace the promoters of said genes such that some of said genes are under the control of a different regulatable promoter.

### Definitions

By "biological pathway" is meant any discrete cell function or process that is carried out by a gene product or a subset of gene products. Biological pathways include anabolic, catabolic, enzymatic, biochemical and metabolic pathways as well as pathways involved in the production of cellular structures such as cell walls. Biological pathways that are usually required for proliferation of cells or microorganisms include, but are not limited to, cell division, DNA synthesis and replication, RNA synthesis (transcription), protein synthesis (translation), protein processing, protein transport, fatty acid biosynthesis, electron transport chains, cell wall synthesis, cell membrane production, synthesis and maintenance, and the like.

By "inhibit activity of a gene or gene product" is meant having the ability to interfere with the function of a gene or gene product in such a way as to decrease expression of the gene, in such a way as to reduce the level or activity of a product of the gene or in such a way as to inhibit the interaction of the gene or gene product with other biological molecules required for its activity. Agents which inhibit the activity of a gene include agents that inhibit transcription of the gene, agents that inhibit processing of the transcript of the gene, agents that reduce the stability of the transcript of the gene, and agents that inhibit translation of the mRNA transcribed from the gene. In microorganisms, agents which inhibit the activity of a gene can act to decrease expression of the operon in which the gene resides or alter the folding or processing of operon RNA so as to reduce the level or activity of the gene product. The gene product can be a non-translated RNA such as ribosomal RNA, a translated RNA (mRNA) or the protein product resulting from translation of the gene mRNA. Of particular utility to the present invention are antisense RNAs that have activities against the operons or genes to which they specifically hybridize.

By "activity against a gene product" is meant having the ability to inhibit the function or to reduce the level or activity of the gene product in a cell. This includes, but is not limited to, inhibiting the enzymatic activity of the gene product or the ability of the gene product to interact with other biological molecules required for its activity, including inhibiting the gene product's assembly into a multimeric structure.

By "activity against a protein" is meant having the ability to inhibit the function or to reduce the level or activity of the protein in a cell. This includes, but is not limited to, inhibiting the enzymatic activity of the protein or the ability of the protein to interact with other biological molecules required for its activity, including inhibiting the protein's assembly into a multimeric structure.

By "activity against a nucleic acid" is meant having the ability to inhibit the function or to reduce the level or activity of the nucleic acid in a cell. This includes, but is not limited to, inhibiting the ability of the nucleic acid interact with other biological molecules required for its activity, including inhibiting the nucleic acid's assembly into a multimeric structure.

By "activity against a gene" is meant having the ability to inhibit the function or expression of the gene in a cell. This includes, but is not limited to, inhibiting the ability of the gene to interact with other biological molecules required for its activity.

By "activity against an operon" is meant having the ability to inhibit the function or reduce the level of one or more products of the operon in a cell. This includes, but is not limited to, inhibiting the enzymatic activity of one or more products of the operon or the ability of one or more products of the operon to interact with other biological molecules required for its activity.

By "antibiotic" is meant an agent which inhibits the proliferation of a cell or microorganism.

By "*E. coli* or *Escherichia coli*" is meant *Escherichia coli* or any organism previously categorized as a species of *Shigella* including *Shigella boydii*, *Shigella flexneri*, *Shigella dysenteriae*, *Shigella sonnei*, *Shigella 2A*.

By "homologous coding nucleic acid" is meant a nucleic acid homologous to a nucleic acid encoding a gene product whose activity or level is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOS.: 1-6213 or a portion thereof. In some embodiments, the homologous coding nucleic acid may have at least 97%, at least 95%, at least 90%, at least 85%, at least 80%, or at least 70% nucleotide sequence identity to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42,397 and fragments comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides thereof. In other embodiments the homologous coding nucleic acids may have at least 97%, at least 95%, at least 90%, at least 85%, at least 80%, or at least 70% nucleotide sequence identity to a nucleotide sequence selected from the group consisting of the nucleotide sequences complementary to one of SEQ ID NOS.: 1-6213 and fragments comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides thereof. Identity may be measured using BLASTN version 2.0 with the default parameters or tBLASTX with the default parameters. (Altschul, S.F. et al. Gapped BLAST and PSI-BLAST: A New Generation of Protein Database Search Programs, Nucleic Acid Res. 25: 3389-3402 (1997). Alternatively a "homologous coding nucleic acid" could be identified by membership of the gene of interest to a functional orthologue cluster. All other members of that orthologue cluster would be considered homologues. Such a library of functional orthologue clusters can be found at <http://www.ncbi.nlm.nih.gov/COG>. A gene can be classified into a cluster of orthologous groups or COG by using the COGNITOR program available at the above web site, or by direct BLASTP comparison of the gene of interest to the members of the COGs and analysis of these results as described by Tatusov, R.L., Galperin, M.Y., Natale, D.A. and Koonin, E.V. (2000) The COG database: a tool for genome-scale analysis of protein functions and evolution. Nucleic Acids Research v. 28 n. 1, pp33-36.

Homologous coding nucleic acids and the homologous polypeptides which they encode may also be identified using a "reciprocal" best-hit analysis. To facilitate the identification of homologous coding nucleic acids and homologous polypeptides, paralogous genes within each of

51 organisms are identified and clustered prior to comparison to other organisms. Briefly, the polypeptide sequence of each polypeptide encoded by each open reading frame (ORF) in a given organism is compared to the polypeptide sequence encoded by every other ORF for that organism for each of the 51 pathogenic organisms (PathoSeq Sept 2001 release) using BLASTP 2.09 algorithm without filtering. Simultaneously, the polypeptide sequence encoded by each ORF of an organism is compared to the polypeptide sequences encoded by each of the ORFs in the remaining 51 organisms. Those polypeptides within a single organism that shared a higher degree of sequence identity to one another than to polypeptide sequences obtained from any other organisms are clustered as "paralog" sequences for "reciprocal" best-hit analysis.

10 For each reference organism, the 50 homologous coding nucleic acids (and the 50 homologous polypeptides which they encode) can be determined by identifying the ORFs in each of the 50 comparison organisms which encode a polypeptide sharing the highest degree of amino acid sequence identity to the polypeptide encoded by the ORF from the reference organism. The accuracy of the identification of the predicted homologous coding nucleic acids (and the 15 homologous polypeptides which they encode) is confirmed by a "reciprocal" BLAST analysis in which the polypeptide sequence of the predicted homologous polypeptide is compared against the polypeptides encoded by each of the ORFS in the reference organism using BLASTP 2.09 algorithm without filtering. Only those polypeptides that share the highest degree of amino acid sequence identity in each portion of the two-way comparison are retained for further analysis.

20 The term "homologous coding nucleic acid" also includes nucleic acids comprising nucleotide sequences which encode polypeptides having at least 99%, 95%, at least 90%, at least 85%, at least 80%, at least 70%, at least 60%, at least 50%, at least 40% or at least 25% amino acid identity or similarity to a polypeptide comprising the amino acid sequence of one of SEQ ID NOs: 42,398-78,581 or to a polypeptide whose expression is inhibited by a nucleic acid comprising a 25 nucleotide sequence of one of SEQ ID NOs: 1-6213 or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof as determined using the FASTA version 3.0t78 algorithm with the default parameters. Alternatively, protein identity or similarity may be identified using BLASTP with the default parameters, BLASTX with the default parameters, TBLASTN with the default parameters, or tBLASTX with the default parameters. 30 (Altschul, S.F. et al. Gapped BLAST and PSI-BLAST: A New Generation of Protein Database Search Programs, Nucleic Acid Res. 25: 3389-3402 (1997).

Additionally, homologous coding nucleic acids and the homologous polypeptides which they encode may be identified using a "reciprocal" best-hit analysis. To facilitate the identification of homologous coding nucleic acids and homologous polypeptides, paralogous genes within each of 35 51 organisms are identified and clustered prior to comparison to other organisms. Briefly, the polypeptide sequence of each polypeptide encoded by each open reading frame (ORF) in a given organism is compared to the polypeptide sequence encoded by every other ORF for that organism for each of the 51 pathogenic organisms (PathoSeq Sept 2001 release) using BLASTP 2.09

algorithm without filtering. Simultaneously, the polypeptide sequence encoded by each ORF of an organism is compared to the polypeptide sequences encoded by each of the ORFs in the remaining 51 organisms. Those polypeptides within a single organism that shared a higher degree of sequence identity to one another than to polypeptide sequences obtained from any other organisms are clustered as "paralog" sequences for "reciprocal" best-hit analysis.

For each reference organism, the 50 homologous coding nucleic acids (and the 50 homologous polypeptides which they encode) can be determined by identifying the ORFs in each of the 50 comparison organisms which encode a polypeptide sharing the highest degree of amino acid sequence identity to the polypeptide encoded by the ORF from the reference organism. The accuracy of the identification of the predicted homologous coding nucleic acids (and the homologous polypeptides which they encode) is confirmed by a "reciprocal" BLAST analysis in which the polypeptide sequence of the predicted homologous polypeptide is compared against the polypeptides encoded by each of the ORFs in the reference organism using BLASTP 2.09 algorithm without filtering. Only those polypeptides that share the highest degree of amino acid sequence identity in each portion of the two-way comparison are retained for further analysis.

The term "homologous coding nucleic acid" also includes coding nucleic acids which hybridize under stringent conditions to a nucleic acid selected from the group consisting of the nucleotide sequences complementary to one of SEQ ID NOS.: 6214-42,397 and coding nucleic acids comprising nucleotide sequences which hybridize under stringent conditions to a fragment comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides of the sequences complementary to one of SEQ ID NOS.: 6214-42,397. As used herein, "stringent conditions" means hybridization to filter-bound nucleic acid in 6xSSC at about 45°C followed by one or more washes in 0.1xSSC/0.2% SDS at about 68°C. Other exemplary stringent conditions may refer, *e.g.*, to washing in 6xSSC/0.05% sodium pyrophosphate at 37°C, 48°C, 55°C, and 60°C as appropriate for the particular probe being used.

The term "homologous coding nucleic acid" also includes coding nucleic acids comprising nucleotide sequences which hybridize under moderate conditions to a nucleotide sequence selected from the group consisting of the sequences complementary to one of SEQ ID NOS.: 6214-42,397 and coding nucleic acids comprising nucleotide sequences which hybridize under moderate conditions to a fragment comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides of the sequences complementary to one of SEQ ID NOS.: 6214-42,397. As used herein, "moderate conditions" means hybridization to filter-bound DNA in 6x sodium chloride/sodium citrate (SSC) at about 45°C followed by one or more washes in 0.2xSSC/0.1% SDS at about 42-65°C.

The term "homologous coding nucleic acids" also includes nucleic acids comprising nucleotide sequences which encode a gene product whose activity may be complemented by a gene encoding a gene product whose activity is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 1-6213. In some embodiments, the



homologous coding nucleic acids may encode a gene product whose activity is complemented by the gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42,397. In other embodiments, the homologous coding nucleic acids may comprise a nucleotide sequence encode a gene product whose activity is complemented by one of the polypeptides of SEQ ID NOs. 42,398-78,581.

The term "homologous antisense nucleic acid" includes nucleic acids comprising a nucleotide sequence having at least 97%, at least 95%, at least 90%, at least 85%, at least 80%, or at least 70% nucleotide sequence identity to a nucleotide sequence selected from the group consisting of one of the sequences of SEQ ID NOS. 1-6213 and fragments comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides thereof. Homologous antisense nucleic acids may also comprising nucleotide sequences which have at least 97%, at least 95%, at least 90%, at least 85%, at least 80%, or at least 70% nucleotide sequence identity to a nucleotide sequence selected from the group consisting of the sequences complementary to one of sequences of SEQ ID NOS.: 6214-42,397 and fragments comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides thereof. Nucleic acid identity may be determined as described above.

The term "homologous antisense nucleic acid" also includes antisense nucleic acids comprising nucleotide sequences which hybridize under stringent conditions to a nucleotide sequence complementary to one of SEQ ID NOs.: 1-6213 and antisense nucleic acids comprising nucleotide sequences which hybridize under stringent conditions to a fragment comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides of the sequence complementary to one of SEQ ID NOs. 1-6213. Homologous antisense nucleic acids also include antisense nucleic acids comprising nucleotide sequences which hybridize under stringent conditions to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42,397 and antisense nucleic acids comprising nucleotide sequences which hybridize under stringent conditions to a fragment comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides of one of SEQ ID NOS.: 6214-42,397.

The term "homologous antisense nucleic acid" also includes antisense nucleic acids comprising nucleotide sequences which hybridize under moderate conditions to a nucleotide sequence complementary to one of SEQ ID NOs.: 1-6213 and antisense nucleic acids comprising nucleotide sequences which hybridize under moderate conditions to a fragment comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides of the sequence complementary to one of SEQ ID NOs. 1-6213. Homologous antisense nucleic acids also include antisense nucleic acids comprising nucleotide sequences which hybridize under moderate conditions to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42,397 and antisense nucleic acids which comprising nucleotide sequences hybridize under moderate conditions to a fragment comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides of one of SEQ ID NOS.: 6214-42,397.

By "homologous polypeptide" is meant a polypeptide homologous to a polypeptide whose activity or level is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 or by a homologous antisense nucleic acid. The term "homologous polypeptide" includes polypeptides having at least 99%, 95%, at least 90%, at least 85%, at least 80%, at least 70%, at least 60%, at least 50%, at least 40% or at least 25% amino acid identity or similarity to a polypeptide whose activity or level is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOs.: 1-6213 or by a homologous antisense nucleic acid, or polypeptides having at least 99%, 95%, at least 90%, at least 85%, at least 80%, at least 70%, at least 60%, at least 50%, at least 40% or at least 25% amino acid identity or similarity to a polypeptide to a fragment comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids of a polypeptide whose activity or level is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOs.: 1-6213 or by a homologous antisense nucleic acid. Identity or similarity may be determined using the FASTA version 3.0t78 algorithm with the default parameters. Alternatively, protein identity or similarity may be identified using BLASTP with the default parameters, BLASTX with the default parameters, or TBLASTN with the default parameters. (Altschul, S.F. et al. Gapped BLAST and PSI-BLAST: A New Generation of Protein Database Search Programs, *Nucleic Acid Res.* 25: 3389-3402 (1997). Additionally, homologous coding nucleic acids and the homologous polypeptides which they encode may be identified using a "reciprocal" best-hit analysis. To facilitate the identification of homologous coding nucleic acids and homologous polypeptides, paralogous genes within each of 51 organisms are identified and clustered prior to comparison to other organisms. Briefly, the polypeptide sequence of each polypeptide encoded by each open reading frame (ORF) in a given organism is compared to the polypeptide sequence encoded by every other ORF for that organism for each of the 51 pathogenic organisms (PathoSeq Sept 2001 release) using BLASTP 2.09 algorithm without filtering. Simultaneously, the polypeptide sequence encoded by each ORF of an organism is compared to the polypeptide sequences encoded by each of the ORFs in the remaining 51 organisms. Those polypeptides within a single organism that shared a higher degree of sequence identity to one another than to polypeptide sequences obtained from any other organisms are clustered as "paralog" sequences for "reciprocal" best-hit analysis.

For each reference organism, the 50 homologous coding nucleic acids (and the 50 homologous polypeptides which they encode) can be determined by identifying the ORFs in each of the 50 comparison organisms which encode a polypeptide sharing the highest degree of amino acid sequence identity to the polypeptide encoded by the ORF from the reference organism. The accuracy of the identification of the predicted homologous coding nucleic acids (and the homologous polypeptides which they encode) is confirmed by a "reciprocal" BLAST analysis in which the polypeptide sequence of the predicted homologous polypeptide is compared against the polypeptides encoded by each of the ORFS in the reference organism using BLASTP 2.09

algorithm without filtering. Only those polypeptides that share the highest degree of amino acid sequence identity in each portion of the two-way comparison are retained for further analysis.

The term homologous polypeptide also includes polypeptides having at least 99%, 95%, at least 90%, at least 85%, at least 80%, at least 70%, at least 60%, at least 50%, at least 40% or at least 25% amino acid identity or similarity to a polypeptide selected from the group consisting of SEQ ID NOs: 42,398-78,581 and polypeptides having at least 99%, 95%, at least 90%, at least 85%, at least 80%, at least 70%, at least 60%, at least 50%, at least 40% or at least 25% amino acid identity or similarity to a fragment comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids of a polypeptide selected from the group consisting of SEQ ID NOs: 42,398-78,581.

The invention also includes polynucleotides, preferably DNA molecules, that hybridize to one of the nucleic acids of SEQ ID NOs.: 1-6213, SEQ ID NOs.: 6214-42,397 or the complements of any of the preceding nucleic acids. Such hybridization may be under stringent or moderate conditions as defined above or under other conditions which permit specific hybridization. The nucleic acid molecules of the invention that hybridize to these DNA sequences include oligodeoxynucleotides ("oligos") which hybridize to the target gene under highly stringent or stringent conditions. In general, for oligos between 14 and 70 nucleotides in length the melting temperature ( $T_m$ ) is calculated using the formula:

$$T_m (^{\circ}\text{C}) = 81.5 + 16.6(\log[\text{monovalent cations (molar)}] + 0.41 (\% \text{ G+C}) - (500/N))$$

where N is the length of the probe. If the hybridization is carried out in a solution containing formamide, the melting temperature may be calculated using the equation:

$$T_m (^{\circ}\text{C}) = 81.5 + 16.6(\log[\text{monovalent cations (molar)}] + 0.41(\% \text{ G+C}) - (0.61) (\% \text{ formamide}) - (500/N))$$

where N is the length of the probe. In general, hybridization is carried out at about 20-25 degrees below  $T_m$  (for DNA-DNA hybrids) or about 10-15 degrees below  $T_m$  (for RNA-DNA hybrids).

Other hybridization conditions are apparent to those of skill in the art (see, for example, Ausubel, F.M. *et al.*, eds., 1989, *Current Protocols in Molecular Biology*, Vol. I, Green Publishing Associates, Inc. and John Wiley & Sons, Inc., New York, at pp. 6.3.1-6.3.6 and 2.10.3.

The term, *Salmonella*, is the generic name for a large group of gram negative enteric bacteria that are closely related to *Escherichia coli*. The diseases caused by *Salmonella* are often due to contamination of foodstuffs or the water supply and affect millions of people each year. Traditional methods of *Salmonella* taxonomy were based on assigning a separate species name to each serologically distinguishable strain (Kauffmann, F 1966 The bacteriology of the *Enterobacteriaceae*. Munksgaard, Copenhagen). Serology of *Salmonella* is based on surface antigens (O [somatic] and H [flagellar]). Over 2,400 serotypes or serovars of *Salmonella* are known (Popoff, et al. 2000 Res. Microbiol. 151:63-65). Therefore, each serotype was considered to

be a separate species and often given names, accordingly (e.g. *S. paratyphi*, *S. typhimurium*, *S. typhi*, *S. enteritidis*, etc.).

However, by the 1970s and 1980s it was recognized that this system was not only cumbersome, but also inaccurate. Then, many *Salmonella* species were lumped into a single species (all serotypes and subgenera I, II, and IV and all serotypes of *Arizona*) with a second subspecies, *S. bongorii* also recognized (Crosa, et al., 1973, J. Bacteriol. 115:307-315). Though species designations are based on the highly variable surface antigens, the *Salmonella* are very similar otherwise with a major exception being pathogenicity determinants.

There has been some debate on the correct name for the *Salmonella* species. Currently (Brenner, et al. 2000 J. Clin. Microbiol. 38:2465-2467), the accepted name is *Salmonella enterica*. *S. enterica* is divided into six subspecies (I, *S. enterica* subsp. *enterica*; II, *S. enterica*, subsp. *salamae*; IIIa, *S. enterica* subsp. *arizonae*; IIIb, *S. enterica* subsp. *diarizonae*; IV, *S. enterica* subsp. *houstenae*; and VI, *S. enterica* subsp. *indica*). Within subspecies I, serotypes are used to distinguish each of the serotypes or serovars (e.g. *S. enterica* serotype Enteritidis, *S. enterica* serotype Typhimurium, *S. enterica* serotype Typhi, and *S. enterica* serotype Choleraesuis, etc.). Current convention is to spell this out on first usage (*Salmonella enterica* ser. Typhimurium) and then use an abbreviated form (*Salmonella* Typhimurium or *S. Typhimurium*). Note, the genus and species names (*Salmonella enterica*) are italicized but not the serotype/serovar name (Typhimurium). Because the taxonomic committees have yet to officially approve of the actual species name, this latter system is what is employed by the CDC (Brenner, et al. 2000 J. Clin. Microbiol. 38:2465-2467). Due to the concerns of both taxonomic priority and medical importance, some of these serotypes might ultimately receive full species designations (*S. typhi* would be the most notable).

Therefore, as used herein "*Salmonella enterica* or *S. enterica*" includes serovars Typhi, Typhimurium, Paratyphi, Choleraesuis, etc." However, appeals of the "official" name are in process and the taxonomic designations may change (*S. choleraesuis* is the species name that could replace *S. enterica* based solely on priority).

By "identifying a compound" is meant to screen one or more compounds in a collection of compounds such as a combinatorial chemical library or other library of chemical compounds or to characterize a single compound by testing the compound in a given assay and determining whether it exhibits the desired activity.

By "inducer" is meant an agent or solution which, when placed in contact with a cell or microorganism, increases transcription, or inhibitor and/or promoter clearance/fidelity, from a desired promoter.

As used herein, "nucleic acid" means DNA, RNA, or modified nucleic acids. Thus, the terminology "the nucleic acid of SEQ ID NO: X" or "the nucleic acid comprising the nucleotide sequence" includes both the DNA sequence of SEQ ID NO: X and an RNA sequence in which the thymidines in the DNA sequence have been substituted with uridines in the RNA sequence and in which the deoxyribose backbone of the DNA sequence has been substituted with a ribose backbone

in the RNA sequence. Modified nucleic acids are nucleic acids having nucleotides or structures which do not occur in nature, such as nucleic acids in which the internucleotide phosphate residues with methylphosphonates, phosphorothioates, phosphoramidates, and phosphate esters. Nonphosphate internucleotide analogs such as siloxane bridges, carbonate bridges, thioester bridges, as well as many others known in the art may also be used in modified nucleic acids. Modified nucleic acids may also comprise,  $\alpha$ -anomeric nucleotide units and modified nucleotides such as 1,2-dideoxy-d-ribofuranose, 1,2-dideoxy-1-phenylribofuranose, and  $N^4$ ,  $N^4$ -ethano-5-methyl-cytosine are contemplated for use in the present invention. Modified nucleic acids may also be peptide nucleic acids in which the entire deoxyribose-phosphate backbone has been exchanged with a chemically completely different, but structurally homologous, polyamide (peptide) backbone containing 2-aminoethyl glycine units.

As used herein, "sub-lethal" means a concentration of an agent below the concentration required to inhibit all cell growth.

#### Brief Description of the Drawings

Figure 1A illustrates a method for replacing a promoter using a promoter replacement cassette comprising a 5' region homologous to the sequence which is 5' of the natural promoter in the chromosome, the promoter which is to replace the chromosomal promoter and a 3' region which is homologous to sequences 3' of the natural promoter in the chromosome.

Figure 1B illustrates a method for replacing a promoter using a promoter replacement cassette comprising a nucleic acid encoding an identifiable or selectable marker disposed between the 5' region which is homologous to the sequence 5' of the natural promoter and the promoter which is to replace the chromosomal promoter and a transcriptional terminator 3' of the gene encoding an identifiable or selectable marker.

Figures 2A and 2B illustrate one method for identifying amplification products which are underrepresented or overrepresented in a culture.

Figures 3A and 3B illustrate another method for identifying amplification products which are underrepresented or overrepresented in a culture.

Figure 4 illustrates the results of a hybridization analysis where the antisense nucleic acid expressed by a strain in the culture is not complementary to all or a portion of the gene encoding the target of the compound (i.e. a nonspecific strain).

Figure 5 illustrates the results of a hybridization analysis where the antisense nucleic acid expressed by a strain in the culture is complementary to all or a portion of the gene encoding the target of the compound, the hybridization intensity for that strain will be intimately correlated with the concentration of the compound (i.e. a specific strain).

Figure 6 illustrates an oligonucleotide comprising a lac operator flanked on each side by 40 nucleotides homologous to the promoter is the promoter which drives expression of the *yabB yabC ftsL ftsI murE* genes in an operon for use in inserting the lac operator into the promoter.

Figure 7 is an IPTG dose response curve in *E. coli* transformed with an IPTG-inducible plasmid containing either an antisense clone to the *E. coli* ribosomal protein *rplW* (AS-*rplW*) which is required for protein synthesis and essential for cell proliferation, or an antisense clone to the *elaD* (AS-*elaD*) gene which is not known to be involved in protein synthesis and which is also essential for proliferation.

Figure 8A is a tetracycline dose response curve in *E. coli* transformed with an IPTG-inducible plasmid containing antisense to *rplW* (AS-*rplW*) in the absence (0) or presence of IPTG at concentrations that result in 20% and 50% growth inhibition.

Figure 8B is a tetracycline dose response curve in *E. coli* transformed with an IPTG-inducible plasmid containing antisense to *elaD* (AS-*elaD*) in the absence (0) or presence of IPTG at concentrations that result in 20% and 50% growth inhibition.

Figure 9 is a graph showing the fold increase in tetracycline sensitivity of *E. coli* transfected with antisense clones to essential ribosomal proteins *L23* (AS-*rplW*) and *L7/L12* and *L10* (AS-*rplLrplJ*). Antisense clones to genes known to not be directly involved in protein synthesis, *atpB/E* (AS-*atpB/E*), *visC* (AS-*visC*), *elaD* (AS-*elaD*), *yohH* (AS-*yohH*), are much less sensitive to tetracycline.

Figure 10 illustrates the results of an assay in which *Staphylococcus aureus* cells transcribing an antisense nucleic acid complementary to the *gyrB* gene encoding the  $\beta$  subunit of gyrase were contacted with several antibiotics whose targets were known.

Figure 11 illustrates a microtitration plate which contains antibiotic and inducer at gradient concentrations in a matrix format in 10 times excess quantity.

Figure 12 illustrates the results of an experiment demonstrating that at appropriate concentrations of inducer, cells which overexpress the *defB* gene product were able to grow at elevated concentrations of the antibiotic actinonin.

Figure 13 illustrates the results of an experiment demonstrating that at appropriate concentrations of inducer cells which overexpress the *folA* gene product were able to grow at elevated concentrations of the antibiotic trimethoprim.

Figure 14 illustrates the results of an experiment demonstrating that overexpression of the *fabI* gene confers resistance to triclosan, which acts on the gene product of the *fabI* gene, but does not confer resistance to cerulenin, trimethoprim, or actinonin, each of which act on other gene products.

Figure 15 illustrates the results of an experiment demonstrating that overexpression of the *folA* gene confers resistance to trimethoprim, which acts on the gene product of the *folA* gene but does not confer resistance to triclosan, cerulenin, or actinonin, each of which act on other gene products.

Figure 16 illustrates the results of an experiment demonstrating that overexpression of the *defB* gene conferred resistance to actinonin, which acts on the gene product of the *defB* gene but

does not confer resistance to cerulenin, trimethoprim, or triclosan, each of which act on other gene products.

Figure 17 illustrates the results of an experiment demonstrating that overexpression of the *fabF* gene conferred resistance to cerulenin, which acts on the gene product of the *fabF* gene,  $\beta$  keto-acyl carrier protein synthase but does not confer resistance to triclosan, trimethoprim, or actinonin, each of which act on other gene products.

Figure 18 illustrates the results of experiments in which a mixture of nine strains was grown wells in a 96 well plate in medium containing various concentrations of inducer and a sufficient concentration of actinonin, cerulenin, triclosan or trimethoprim to inhibit the growth of strains which do not overexpress the targets of these antibiotics.

#### Detailed Description of Embodiments of the Invention

The present invention describes a group of prokaryotic genes and gene families required for cellular proliferation. Exemplary genes and gene families from *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholera* and *Yersinia pestis* are provided. A proliferation-required gene or gene family is one where, in the absence or substantial reduction of a gene transcript and/or gene product, growth or viability of the cell or microorganism is reduced or eliminated. Thus, as used herein, the terminology "proliferation-required" or "required for proliferation" encompasses instances where the absence or substantial reduction of a gene transcript and/or gene product completely eliminates cell growth as well as instances where the absence of a gene transcript and/or gene product merely reduces cell growth. These proliferation-required genes can be used as potential targets for the generation of new antimicrobial agents. To achieve that goal, the present invention also encompasses assays for analyzing proliferation-required genes and for identifying compounds which interact with the gene and/or gene products of the proliferation-required genes. In addition, the present invention contemplates the expression of genes and the purification of the proteins encoded by the nucleic acid sequences identified as required proliferation genes and reported herein. The purified proteins can be

used to generate reagents and screen small molecule libraries or other candidate compound libraries for compounds that can be further developed to yield novel antimicrobial compounds.

The present invention also describes methods for identification of nucleotide sequences homologous to these genes and polypeptides described herein, including nucleic acids comprising nucleotide sequences homologous to the nucleic acids of SEQ ID NOS.: 6214-42397 and polypeptides homologous to the polypeptides of SEQ ID NOs.: 42398-78581. For example, these sequences may be used to identify homologous coding nucleic acids, homologous antisense nucleic acids, or homologous polypeptides in microorganisms such as *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* or any species falling within the genera of any of the above species. In some embodiments, the homologous coding nucleic acids, homologous antisense nucleic acids, or homologous polypeptides are identified in an organism other than *E. coli*.

The homologous coding nucleic acids, homologous antisense nucleic acids, or homologous polypeptides, may then be used in each of the methods described herein, including methods of identifying compounds which inhibit the proliferation of the organism containing the homologous coding nucleic acid, homologous antisense nucleic acid or homologous polypeptide, methods of inhibiting the growth of the organism containing the homologous coding nucleic acid, homologous antisense nucleic acid or homologous polypeptide, methods of identifying compounds which influence the activity or level of a gene product required for proliferation of the organism containing the homologous coding nucleic acid, homologous antisense nucleic acid or homologous



polypeptide, methods for identifying compounds or nucleic acids having the ability to reduce the level or activity of a gene product required for proliferation of the organism containing the homologous coding nucleic acid, homologous antisense nucleic acid or homologous polypeptide, methods of inhibiting the activity or expression of a gene in an operon required for proliferation of the organism containing the homologous coding nucleic acid, homologous antisense nucleic acid or homologous polypeptide, methods for identifying a gene required for proliferation of the organism containing the homologous coding nucleic acid, homologous antisense nucleic acid or homologous polypeptide, methods for identifying the biological pathway in which a gene or gene product required for proliferation of the organism containing the homologous coding nucleic acid, homologous antisense nucleic acid or homologous polypeptide lies, methods for identifying compounds having activity against biological pathway required for proliferation of the organism containing the homologous coding nucleic acid, homologous antisense nucleic acid or homologous polypeptide, methods for determining the biological pathway on which a test compound acts in the organism containing the homologous coding nucleic acid, homologous antisense nucleic acid or homologous polypeptide, methods of replacing an endogenous promoter with a regulatable promoter which controls the expression of the homologous coding nucleic acid, homologous antisense nucleic acid or homologous polypeptide, methods of inserting an operator within or near an endogenous promoter to provide regulatable expression of the homologous coding nucleic acid, homologous antisense nucleic acid or homologous polypeptide, methods of identifying the target on which a compound acts in the organism containing the homologous coding nucleic acid, homologous antisense nucleic acid or homologous polypeptide, and methods of inhibiting the proliferation of the organism containing the homologous coding nucleic acid, homologous antisense nucleic acid or homologous polypeptide in a subject. In some embodiments of the present invention, the methods are performed using an organism, other than *E. coli* or a gene or gene product from an organism other than *E. coli*.

One embodiment of the present invention utilizes a novel method to identify proliferation-required sequences. Generally, a library of nucleic acid sequences from a given source are subcloned or otherwise inserted immediately downstream of an inducible promoter on an appropriate vector, such as a *Staphylococcus aureus*/*E. coli* or *Pseudomonas aeruginosa*/*E. coli* shuttle vector, or a vector which will replicate in both *Salmonella typhimurium* and *Klebsiella pneumoniae*, or other vector or shuttle vector capable of functioning in the intended organism, thus forming an expression library. It is generally preferred that expression is directed by a regulatable promoter sequence such that expression level can be adjusted by addition of variable concentrations of an inducer molecule or of an inhibitor molecule to the medium. For example, a number of regulatable promoters useful for regulating the expression of nucleic acid sequences over a wide range of expression levels are described in U.S. Patent Application Serial Number 10/032,393, filed December 21, 2001. Temperature activated promoters, such as promoters regulated by temperature sensitive repressors, such as the lambda C<sub>1857</sub> repressor, are also envisioned. Although the insert nucleic acids may be derived from the chromosome

of the cell or microorganism into which the expression vector is to be introduced, because the insert is not in its natural chromosomal location, the insert nucleic acid is an exogenous nucleic acid for the purposes of the discussion herein. The term "expression" is defined as the production of a sense or antisense RNA molecule from a gene, gene fragment, genomic fragment, chromosome, operon or  
5 portion thereof. Expression can also be used to refer to the process of peptide or polypeptide synthesis. An expression vector is defined as a vehicle by which a ribonucleic acid (RNA) sequence is transcribed from a nucleic acid sequence carried within the expression vehicle. The expression vector can also contain features that permit translation of a protein product from the transcribed RNA message expressed from the exogenous nucleic acid sequence carried by the expression vector. Accordingly, an  
10 expression vector can produce an RNA molecule as its sole product or the expression vector can produce a RNA molecule that is ultimately translated into a protein product.

Once generated, the expression library containing the exogenous nucleic acid sequences is introduced into a population of cells (such as the organism from which the exogenous nucleic acid sequences were obtained) to search for genes that are required for bacterial proliferation. Because the  
15 library molecules are foreign, in context, to the population of cells, the expression vectors and the nucleic acid segments contained therein are considered exogenous nucleic acid.

Expression of the exogenous nucleic acid fragments in the test population of cells containing the expression library is then activated. Activation of the expression vectors consists of subjecting the cells containing the vectors to conditions that result in the expression of the exogenous nucleic acid  
20 sequences carried by the expression library. The test population of cells is then assayed to determine the effect of expressing the exogenous nucleic acid fragments on the test population of cells. Those expression vectors that negatively impact the growth of the cells upon induction of expression of the random sequences contained therein are identified, isolated, and purified for further study.

In some embodiments, vectors which comprises a regulatable fusion promoter selected  
25 from a suite of fusion promoters, wherein the promoter suite is useful for modulating both the basal and maximal levels of transcription of a nucleic acid over a wide dynamic range thus allowing the desired level of production of a transcript, can be used to express exogenous nucleic acids, including the nucleic acids of the present invention. Such promoters are described in U.S. Patent Application Serial Number 10/032,393, filed December 21, 2001, the disclosure of which is  
30 incorporated herein by reference in its entirety.

In some other embodiments, vectors useful for the production of stabilized mRNA having an increased lifetime (including antisense RNA) in Gram negative organisms are described in U.S. Provisional Patent Application Serial Number 60/343,512, filed December 21, 2001. Briefly, the stabilized antisense RNA may comprise an antisense RNA which was identified as inhibiting  
35 proliferation as described above which has been engineered to contain at least one stem loop flanking each end of the antisense nucleic acid. In some embodiments, the at least one stem-loop structure formed at the 5' end of the stabilized antisense nucleic acid comprises a flush, double stranded 5' end. In some embodiments, one or more of the stem loops comprises a rho independent

terminator. In additional embodiments, the stabilized antisense RNA lacks a ribosome binding site. In further embodiments, the stabilized RNA lacks sites which are cleaved by one or more RNases, such as RNase E or RNase III. In some embodiments, the stabilized antisense RNA may be transcribed in a cell which the activity of at least one enzyme involved in RNA degradation has been reduced. For example, the activity of an enzyme such as RNase E, RNase II, RNase III, polynucleotide phosphorylase, and poly(A) polymerase, RNA helicase, enolase or an enzyme having similar functions may be reduced in the cell.

Alternatively, genes required for proliferation may be identified by replacing the natural promoter for the proliferation required gene with a regulatable promoter as described above. The growth of such strains under conditions in which the promoter is active or non-repressed is compared to the growth under conditions in which the promoter is inactive or repressed. If the strains fail to grow or grow at a substantially reduced rate under conditions in which the promoter is inactive or repressed but grow normally under conditions in which the promoter is active or non-repressed, then the gene which is operably linked to the regulatable promoter encodes a gene product required for proliferation. For example, proliferation-required genes and gene products identified using promoter replacement are described in U.S. Patent Application Serial Number 09/948,993.

For example, in some embodiments, the natural promoter may be replaced using techniques which employ homologous recombination to exchange a promoter present on the chromosome of the cell with the desired promoter. In such methodology, a nucleic acid comprising a promoter replacement cassette is introduced into the cell. As illustrated in Figure 1A, the promoter replacement cassette comprises a 5' region homologous to the sequence which is 5' of the natural promoter in the chromosome, the promoter which is to replace the chromosomal promoter and a 3' region which is homologous to sequences 3' of the natural promoter in the chromosome. In some embodiments, the promoter replacement cassette may also include a nucleic acid encoding an identifiable or selectable marker disposed between the 5' region which is homologous to the sequence 5' of the natural promoter and the promoter which is to replace the chromosomal promoter. If desired, the promoter replacement cassette may also contain a transcriptional terminator 3' of the gene encoding an identifiable or selectable marker, as illustrated in Figure 1B. As illustrated in Figure 1A and 1B, homologous recombination is allowed to occur between the chromosomal region containing the natural promoter and the promoter replacement cassette. Cells in which the promoter replacement cassette has integrated into the chromosome are identified or selected. To confirm that homologous recombination has occurred, the chromosomal structure of the cells may be verified by Southern analysis or PCR.

In some embodiments, the promoter replacement cassette may be introduced into the cell as a linear nucleic acid, such a PCR product or a restriction fragment. Alternatively, the promoter replacement may be introduced into the cell on a plasmid. Figures 1A and 1B illustrates the

replacement of a chromosomal promoter with a desired promoter through homologous recombination.

In some embodiments, the cell into which the promoter replacement cassette is introduced may carry mutations which enhance its ability to be transformed with linear DNA or which enhance the frequency of homologous recombination. For example, if the cell is an *Escherichia coli* cell it may have a mutation in the gene encoding Exonuclease V of the RecBCD recombination complex. If the cell is an *Escherichia coli* cell it may have a mutation that activates the RecET recombinase of the  $\lambda$  prophage and/or a mutation that enhances recombination through the RecF pathway. For example, the *Escherichia coli* cells may be RecB or RecC mutants carrying an sbcA or sbcB mutation. Alternatively, the *Escherichia coli* cells may be recD mutants. In other embodiments the *Escherichia coli* cells may express the  $\lambda$  Red recombination genes. For example, *Escherichia coli* cells suitable for use in techniques employing homologous recombination have been described in Datsenko, K.A. and Wanner, B.L., PNAS 97:6640-6645 (2000); Murphy, K.C., J. Bact 180: 2053-2071 (1998); Zhang, Y., et al., Nature Genetics 20: 123-128 (1998); and Muirers, J.P.P. et al., Genes & Development 14: 1971-1982 (2000). It will be appreciated that cells carrying mutations in similar genes may be constructed in organisms other than *Escherichia coli*.

In some embodiments of the present invention, a regulatable fusion promoter selected from a suite of fusion promoters, wherein the promoter suite is useful for modulating both the basal and maximal levels of transcription of a nucleic acid over a wide dynamic range thus allowing the desired level of production of a transcript, is with the promoter replacement methods described above. Such promoters are described in U.S. Patent Application Serial Number 10/032,393, filed December 21, 2001, the disclosure of which is incorporated herein by reference in its entirety.

A variety of assays are contemplated to identify nucleic acid sequences that negatively impact growth upon expression. In one embodiment, growth in cultures expressing exogenous nucleic acid sequences and growth in cultures not expressing these sequences is compared. Growth measurements are assayed by examining the extent of growth by measuring optical densities. Alternatively, enzymatic assays can be used to measure bacterial growth rates to identify exogenous nucleic acid sequences of interest. Colony size, colony morphology, and cell morphology are additional factors used to evaluate growth of the host cells. Those cultures that fail to grow or grow at a reduced rate under expression conditions are identified as containing an expression vector encoding a nucleic acid fragment that negatively affects a proliferation-required gene.

Once exogenous nucleic acids of interest are identified, they are analyzed. The first step of the analysis is to acquire the nucleotide sequence of the nucleic acid fragment of interest. To achieve this end, the insert in those expression vectors identified as containing a nucleotide sequence of interest is sequenced, using standard techniques well known in the art. The next step of the process is to determine the source of the nucleotide sequence. As used herein "source" means the genomic region containing the cloned fragment.

Determination of the gene(s) corresponding to the nucleotide sequence is achieved by comparing the obtained sequence data with databases containing known protein and nucleotide sequences from various microorganisms. Thus, initial gene identification is made on the basis of significant sequence similarity or identity to either characterized or predicted *Escherichia coli*,  
 5 *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Salmonella typhimurium* genes or their encoded proteins and/or homologues in other species.

The number of nucleotide and protein sequences available in database systems has been growing exponentially for years. For example, the complete nucleotide sequences of *Caenorhabditis elegans* and several bacterial genomes, including *E. coli*, *Aeropyrum pernix*, *Aquifex aeolicus*,  
 10 *Archaeoglobus fulgidus*, *Bacillus subtilis*, *Borrelia burgdorferi*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium tetani*, *Corynebacterium diphtheria*, *Deinococcus radiodurans*, *Haemophilus influenzae*, *Helicobacter pylori* 26695, *Helicobacter pylori* J99, *Methanobacterium thermoautotrophicum*, *Methanococcus jannaschii*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Pseudomonas aeruginosa*, *Pyrococcus abyssi*, *Pyrococcus horikoshii*,  
 15 *Rickettsia prowazekii*, *Synechocystis PCC6803*, *Thermotoga maritima*, *Treponema pallidum*, *Bordetella pertussis*, *Campylobacter jejuni*, *Clostridium acetobutylicum*, *Mycobacterium tuberculosis* CSU#93, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pseudomonas aeruginosa*, *Pyrobaculum aerophilum*, *Pyrococcus furiosus*, *Rhodobacter capsulatus*, *Salmonella typhimurium*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Ureaplasma urealyticum* and *Vibrio cholera* are available. This nucleotide sequence information is stored in a number of databanks, such as GenBank,  
 20 the National Center for Biotechnology Information (NCBI), the Genome Sequencing Center (<http://genome.wustl.edu/gsc/salmonella.shtml>), and the Sanger Centre ([http://www.sanger.ac.uk/projects/S\\_\\_typhi](http://www.sanger.ac.uk/projects/S__typhi)) which are publicly available for searching. A variety of computer programs are available to assist in the analysis of the sequences stored within these  
 25 databases. FASTA, (W. R. Pearson (1990) "Rapid and Sensitive Sequence Comparison with FASTP and FASTA" Methods in Enzymology 183:63- 98), Sequence Retrieval System (SRS), (Etzold & Argos, SRS an indexing and retrieval tool for flat file data libraries. Comput. Appl. Biosci. 9:49-57, 1993) are two examples of computer programs that can be used to analyze sequences of interest. In one embodiment of the present invention, the BLAST family of computer  
 30 programs, which includes BLASTN version 2.0 with the default parameters, or BLASTX version 2.0 with the default parameters, is used to analyze nucleotide sequences.

BLAST, an acronym for "Basic Local Alignment Search Tool," is a family of programs for database similarity searching. The BLAST family of programs includes: BLASTN, a nucleotide sequence database searching program, BLASTX, a protein database searching program where the input  
 35 is a nucleic acid sequence; and BLASTP, a protein database searching program. BLAST programs embody a fast algorithm for sequence matching, rigorous statistical methods for judging the significance of matches, and various options for tailoring the program for special situations. Assistance

in using the program can be obtained by e-mail at [blast@ncbi.nlm.nih.gov](mailto:blast@ncbi.nlm.nih.gov). tBLASTX can be used to translate a nucleotide sequence in all three potential reading frames into an amino acid sequence.

Bacterial genes are often transcribed in polycistronic groups. These groups comprise operons, which are a collection of genes and intergenic sequences under common regulation. The genes of an operon are transcribed on the same mRNA and are often related functionally. Given the nature of the screening protocol, it is possible that the identified exogenous nucleic acid corresponds to a gene or portion thereof with or without adjacent noncoding sequences, an intragenic sequence (i.e. a sequence within a gene), an intergenic sequence (i.e. a sequence between genes), a nucleotide sequence spanning at least a portion of two or more genes, a 5' noncoding region or a 3' noncoding region located upstream or downstream from the actual nucleotide sequence that is required for bacterial proliferation. Accordingly, it is often desirable to determine which gene(s) that is encoded within the operon is individually required for proliferation.

In one embodiment of the present invention, an operon is identified and then dissected to determine which gene or genes are required for proliferation. Operons can be identified by a variety of means known to those in the art. For example, the RegulonDB DataBase described by Huerta et al. (*Nucl. Acids Res.* 26:55-59, 1998), which may also be found on the website [http://www.cifn.unam.mx/Computational\\_Biology/regulondb/](http://www.cifn.unam.mx/Computational_Biology/regulondb/), provides information about operons in *Escherichia coli*. The Subtilist database (<http://bioweb.pasteur.fr/GenoList/SubtiList>), (Moszer, I., Glaser, P. and Danchin, A. (1995) *Microbiology* 141: 261-268 and Moszer, I (1998) *FEBS Letters* 430: 28-36, may also be used to predict operons. This database lists genes from the fully sequenced, Gram positive bacteria, *Bacillus subtilis*, together with predicted promoters and terminator sites. This information can be used in conjunction with the *Staphylococcus aureus* genomic sequence data to predict operons and thus produce a list of the genes affected by the antisense nucleic acids of the present invention. The *Pseudomonas aeruginosa* web site (<http://www.pseudomonas.com>) can be used to help predict operon organization in this bacterium. The databases available from the Genome Sequencing Center (<http://genome.wustl.edu/gsc/salmonella.shtml>), and the Sanger Centre ([http://www.sanger.ac.uk/projects/S\\_\\_typhi](http://www.sanger.ac.uk/projects/S__typhi)) may be used to predict operons in *Salmonella typhimurium*. The TIGR microbial database has an incomplete version of the *E. faecalis* genome ([http://www.tigr.org/cgi-bin/BlastSearch/blast.cgi?organism=e\\_faecalis](http://www.tigr.org/cgi-bin/BlastSearch/blast.cgi?organism=e_faecalis)). One can take a nucleotide sequence and BLAST it for homologs.

A number of techniques that are well known in the art can be used to dissect the operon. Analysis of RNA transcripts by Northern blot or primer extension techniques are commonly used to analyze operon transcripts. In one aspect of this embodiment, gene disruption by homologous recombination is used to individually inactivate the genes of an operon that is thought to contain a gene required for proliferation.

Several gene disruption techniques have been described for the replacement of a functional gene with a mutated, non-functional (null) allele. These techniques generally involve the use of

homologous recombination. One technique using homologous recombination in *Staphylococcus aureus* is described in Xia et al., 1999, Plasmid 42: 144-149. This technique uses crossover PCR to create a null allele with an in-frame deletion of the coding region of a target gene. The null allele is constructed in such a way that nucleotide sequences adjacent to the wild type gene are retained.

5 These homologous sequences surrounding the deletion null allele provide targets for homologous recombination so that the wild type gene on the *Staphylococcus aureus* chromosome can be replaced by the constructed null allele. This method can be used with other bacteria as well, including *Salmonella* and *Klebsiella* species. Similar gene disruption methods that employ the counter selectable marker *sacB* (Schweizer, H. P., Klassen, T. and Hoang, T. (1996) Mol. Biol. of

10 *Pseudomonas*. ASM press, 229-237, are available for *Pseudomonas*, *Salmonella* and *Klebsiella* species. *E. faecalis* genes can be disrupted by recombining in a non-replicating plasmid that contains an internal fragment to that gene (Leboeuf, C., L. Leblanc, Y. Auffray and A. Hartke. 2000. J. Bacteriol. 182:5799-5806.

The crossover PCR amplification product is subcloned into a suitable vector having a

15 selectable marker, such as a drug resistance marker. In some embodiments the vector may have an origin of replication which is functional in *E. coli* or another organism distinct from the organism in which homologous recombination is to occur, allowing the plasmid to be grown in *E. coli* or the organism other than that in which homologous recombination is to occur, but may lack an origin of replication functional in *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella*

20 *pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus faecium*,

25 *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*, *Staphylococcus epidermidis*,

30 *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae* or *Yersinia pestis* such that selection of the selectable marker requires integration of the vector into the homologous region of the *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter*

35 *baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus*

*faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae* or *Yersinia pestis* chromosome. Usually a single crossover event is responsible for this integration event such that the *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae* or *Yersinia pestis* chromosome now contains a tandem duplication of the target gene consisting of one wild type allele and one deletion null allele separated by vector sequence. Subsequent resolution of the duplication results in both removal of the vector sequence and either restoration of the wild type gene or replacement by the in-frame deletion. The latter outcome will not occur if the gene should prove essential. A more detailed description of this method is provided in Example 10 below. It will be appreciated that this method may be practiced with any of the nucleic acids or organisms described herein.

Recombinant DNA techniques can be used to express the entire coding sequences of the gene identified as required for proliferation, or portions thereof. The over-expressed proteins can be used as reagents for further study. The identified exogenous sequences are isolated, purified, and cloned into a suitable expression vector using methods well known in the art. If desired, the nucleic acids can contain the nucleotide sequences encoding a signal peptide to facilitate secretion of the expressed protein.

Expression of fragments of the bacterial genes identified as required for proliferation is also contemplated by the present invention. The fragments of the identified genes can encode a polypeptide comprising at least 5, at least 10, at least 15, at least 20, at least 25, at least 30, at least 35, at least 40, at least 45, at least 50, at least 55, at least 60, at least 65, at least 75, or more than 75 consecutive amino



acids of a gene complementary to one of the identified sequences of the present invention. The nucleic acids inserted into the expression vectors can also contain endogenous sequences upstream and downstream of the coding sequence.

When expressing the encoded protein of the identified nucleic acid required for bacterial proliferation or a fragment thereof, the nucleic acid to be expressed is operably linked to a promoter in an expression vector using conventional cloning technology. The expression vector can be any of the bacterial, insect, yeast, or mammalian expression systems known in the art. Commercially available vectors and expression systems are available from a variety of suppliers including Genetics Institute (Cambridge, MA), Stratagene (La Jolla, California), Promega (Madison, Wisconsin), and Invitrogen (San Diego, California). If desired, to enhance expression and facilitate proper protein folding, the codon usage and codon bias of the sequence can be optimized for the particular expression organism in which the expression vector is introduced, as explained by Hatfield, et al., U.S. Patent No. 5,082,767, incorporated herein by this reference. Fusion protein expression systems are also contemplated by the present invention.

Following expression of the protein encoded by the identified exogenous nucleic acid, the protein may be purified. Protein purification techniques are well known in the art. Proteins encoded and expressed from identified exogenous nucleic acids can be partially purified using precipitation techniques, such as precipitation with polyethylene glycol. Alternatively, epitope tagging of the protein can be used to allow simple one step purification of the protein. In addition, chromatographic methods such as ion-exchange chromatography, gel filtration, use of hydroxyapatite columns, immobilized reactive dyes, chromatofocusing, and use of high-performance liquid chromatography, may also be used to purify the protein. Electrophoretic methods such as one-dimensional gel electrophoresis, high-resolution two-dimensional polyacrylamide electrophoresis, isoelectric focusing, and others are contemplated as purification methods. Also, affinity chromatographic methods, comprising antibody columns, ligand presenting columns and other affinity chromatographic matrices are contemplated as purification methods in the present invention.

The purified proteins produced from the gene encoding sequences identified as required for proliferation can be used in a variety of protocols to generate useful antimicrobial reagents. In one embodiment of the present invention, antibodies are generated against the proteins expressed from the identified exogenous nucleic acids. Both monoclonal and polyclonal antibodies can be generated against the expressed proteins. Methods for generating monoclonal and polyclonal antibodies are well known in the art. Also, antibody fragment preparations prepared from the produced antibodies discussed above are contemplated.

In addition, the purified protein, fragments thereof, or derivatives thereof may be administered to an individual in a pharmaceutically acceptable carrier to induce an immune response against the protein. Preferably, the immune response is a protective immune response which protects the individual. Methods for determining appropriate dosages of the protein and pharmaceutically acceptable carriers may be determined empirically and are familiar to those skilled in the art.

Another application for the purified proteins of the present invention is to screen small molecule libraries for candidate compounds active against the various target proteins of the present invention. Advances in the field of combinatorial chemistry provide methods, well known in the art, to produce large numbers of candidate compounds that can have a binding, or otherwise inhibitory effect on a target protein. Accordingly, the screening of small molecule libraries for compounds with binding affinity or inhibitory activity for a target protein produced from an identified gene is contemplated by the present invention.

In some embodiments of the present invention, a cell sensitized by expressing an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, an antisense nucleic acid comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides of a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a nucleic acid complementary to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 6214-42397, a nucleic acid complementary to a nucleic acid comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides of a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 6214-42397, a nucleic acid complementary to a nucleic acid which encodes a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42398-78581, a nucleic acid complementary to a nucleic acid which encodes at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids of a polypeptide sequence selected from the group consisting of SEQ ID NOs.: 42398-78581, a homologous antisense nucleic acid, an antisense nucleic acid comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides of a homologous nucleic acid, a nucleic acid complementary to a homologous coding nucleic acid, a nucleic acid complementary to at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides of a homologous coding nucleic acid, a nucleic acid complementary to a nucleic acid which encodes a homologous polypeptide, or a nucleic acid complementary to a nucleic acid which encodes at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids of a homologous polypeptide, is contacted with one or more candidate compounds from a small molecule library. Candidate compounds which further inhibit the proliferation of the sensitized cell may be identified as possessing inhibitory activity for a target protein or product produced by the gene to which the antisense sequence is complementary.

A number of vectors useful in the above methods are described in U.S. Patent Application Serial Number 10/032,393, filed December 21, 2001.

In some embodiments of the present invention, the methods for the production of stabilized RNA, as described in U.S. Patent Application Serial Number 60/343,512, can be used for the production of a stabilized transcript, which corresponds to a nucleic acid described herein, having an increased lifetime in Gram-negative organisms. Briefly, the stabilized antisense RNA may comprise an antisense RNA which was identified as inhibiting proliferation as described above

which has been engineered to contain at least one stem loop flanking each end of the antisense nucleic acid. In some embodiments, the at least one stem-loop structure formed at the 5' end of the stabilized antisense nucleic acid comprises a flush, double stranded 5' end. In some embodiments, one or more of the stem loops comprises a rho independent terminator. In additional embodiments, the stabilized antisense RNA lacks a ribosome binding site. In further embodiments, the stabilized RNA lacks sites which are cleaved by one or more RNases, such as RNase E or RNase III. In some embodiments, the stabilized antisense RNA may be transcribed in a cell which the activity of at least one enzyme involved in RNA degradation has been reduced. For example, the activity of an enzyme such as RNase E, RNase II, RNase III, polynucleotide phosphorylase, and poly(A) polymerase, RNA helicase, enolase or an enzyme having similar functions may be reduced in the cell.

The present invention further contemplates utility against a variety of other pathogenic microorganisms in addition to *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae* and *Yersinia pestis*. For example, homologous coding nucleic acids, homologous antisense nucleic acids or homologous polypeptides from other pathogenic microorganisms (including nucleic acids homologous to the nucleic acids of SEQ ID NOs.: 6214-42397, nucleic acids homologous to the antisense nucleic acids of SEQ ID NOs.: 1-6213, and polypeptides homologous to the polypeptides of SEQ ID NOs.: 42398-78581) may be identified using methods such as those described herein. The homologous coding nucleic acids, homologous antisense nucleic acids or homologous polypeptides may be used to identify compounds which inhibit the proliferation of these other pathogenic microorganisms using methods such as those described herein.

For example, the proliferation-required nucleic acids, antisense nucleic acids, and polypeptides from *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia*

*pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*,  
 5 *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae* or  
 10 *Yersinia pestis* described herein (including the nucleic acids of SEQ ID NOs.: 6214-42397, the antisense nucleic acids of SEQ ID NOs.: 1-6213, and the polypeptides of SEQ ID NOs.: 42398-78581) may be used to identify homologous coding nucleic acids, homologous antisense nucleic acids or homologous polypeptides required for proliferation in prokaryotes and eukaryotes. For example, nucleic acids or polypeptides required for the proliferation of protists, such as *Plasmodium* spp.;  
 15 plants; animals, such as *Entamoeba* spp. and *Contracaecum* spp; and fungi including *Candida* spp., (e.g., *Candida albicans*), *Cryptococcus neoformans*, and *Aspergillus fumigatus* may be identified. In one embodiment of the present invention, monera, specifically bacteria, including both Gram positive and Gram negative bacteria, are probed in search of novel gene sequences required for proliferation. Likewise, homologous antisense nucleic acids which may be used to inhibit growth of these organisms  
 20 or to identify antibiotics may also be identified. These embodiments are particularly important given the rise of drug resistant bacteria.

The number of bacterial species that are becoming resistant to existing antibiotics is growing. A partial list of these microorganisms includes: *Escherichia* spp., such as *E. coli*, *Enterococcus* spp., such as *E. faecalis*; *Pseudomonas* spp., such as *P. aeruginosa*, *Clostridium* spp., such as *C.*  
 25 *botulinum*, *Haemophilus* spp., such as *H. influenzae*, *Enterobacter* spp., such as *E. cloacae*, *Vibrio* spp., such as *V. cholera*; *Moraxella* spp., such as *M. catarrhalis*; *Streptococcus* spp., such as *S. pneumoniae*, *Neisseria* spp., such as *N. gonorrhoeae*; *Mycoplasma* spp., such as *Mycoplasma pneumoniae*; *Salmonella typhimurium*; *Helicobacter pylori*; *Escherichia coli*; and *Mycobacterium tuberculosis*. The genes and polypeptides identified as required for the proliferation of *Escherichia*  
 30 *coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium*  
 35 *diphtheriae*, *Enterobacter cloacae*, *Enterococcus faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella*

*multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*,  
*Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus*  
*mutans*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma*  
*urealyticum*, *Vibrio cholerae* or *Yersinia pestis* (including the nucleic acids of SEQ ID NOs.: 6214-  
5 42397, the sequences complementary to the nucleic acids of SEQ ID NOs.: 6214-42397, and the  
polypeptides of SEQ ID NOs.: 42398-78581) can be used to identify homologous coding nucleic  
acids or homologous polypeptides required for proliferation from these and other organisms using  
methods such as nucleic acid hybridization and computer database analysis. Likewise, the  
antisense nucleic acids which inhibit proliferation of *Escherichia coli*, *Staphylococcus aureus*,  
10 *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*,  
*Acinetobacter baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia*  
*burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter*  
*jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium*  
*botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus*  
15 *faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria*  
*monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*,  
*Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma*  
*pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus*  
*mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*,  
20 *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus*  
*pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio*  
*cholerae* or *Yersinia pestis* (including the antisense nucleic acids of SEQ ID NOs.: 1-6213 or the  
sequences complementary thereto) may also be used to identify antisense nucleic acids which  
inhibit proliferation of these and other microorganisms or cells using nucleic acid hybridization or  
25 computer database analysis.

In one embodiment of the present invention, the nucleic acid sequences from *Escherichia coli*,  
*Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*,  
*Salmonella typhimurium*, *Acinetobacter baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*,  
*Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*,  
30 *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*,  
*Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium*  
*diphtheriae*, *Enterobacter cloacae*, *Enterococcus faecium*, *Haemophilus influenzae*, *Helicobacter*  
*pylori*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium*  
*avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma*  
35 *genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella*  
*multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*,  
*Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus*  
*mutans*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma*

urealyticum, *Vibrio cholerae* or *Yersinia pestis* (including the nucleic acids of SEQ ID NOs.: 6214-42397 and the antisense nucleic acids of SEQ ID NOs. 1-6213) are used to screen genomic libraries generated from *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter baumannii*,  
5 *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria monocytogenes*,  
10 *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus pneumoniae*,  
15 *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Yersinia pestis* and other bacterial species of interest. For example, the genomic library may be from Gram positive bacteria, Gram negative bacteria or other organisms including *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*,  
20 *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*,  
25 *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*,  
30 *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* or any species falling within the genera of any of the above species, including coagulase negative species of *Staphylococcus*. In some embodiments, the genomic

library may be from an organism other than *E. coli*. Standard molecular biology techniques are used to generate genomic libraries from various cells or microorganisms. In one aspect, the libraries are generated and bound to nitrocellulose paper. The identified exogenous nucleic acid sequences of the present invention can then be used as probes to screen the libraries for homologous sequences.

5 For example, the libraries may be screened to identify homologous coding nucleic acids or homologous antisense nucleic acids comprising nucleotide sequences which hybridize under stringent conditions to a nucleic acid selected from the group consisting of SEQ ID NOS.: 1-6213, nucleic acids comprising nucleotide sequences which hybridize under stringent conditions to a fragment comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500  
10 consecutive nucleotides of one of SEQ ID NOS. 1-6213, nucleic acids comprising nucleotide sequences which hybridize under stringent conditions to a nucleic acid complementary to one of SEQ ID NOS. 1-6213, nucleic acids comprising nucleotide sequences which hybridize under stringent conditions to a fragment comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides of the sequence complementary to one of SEQ ID NOS. 1-  
15 6213, nucleic acids comprising nucleotide sequences which hybridize under stringent conditions to a nucleic acid selected from the group consisting of SEQ ID NOS.: 6214-42397, nucleic acids comprising nucleotide sequences which hybridize under stringent conditions to a fragment comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides of one of SEQ ID NOS.: 6214-42397, nucleic acids comprising nucleotide sequences  
20 which hybridize under stringent conditions to a nucleic acid complementary to one of SEQ ID NOS.: 6214-42397, nucleic acids comprising nucleotide sequences which hybridize under stringent conditions to a fragment comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides of the sequence complementary to one of SEQ ID NOS.: 6214-42397.

25 The libraries may also be screened to identify homologous nucleic coding nucleic acids or homologous antisense nucleic acids comprising nucleotide sequences which hybridize under moderate conditions to a nucleic acid selected from the group consisting of SEQ ID NOS.: 1-6213, nucleic acids comprising nucleotide sequences which hybridize under moderate conditions to a fragment comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500  
30 consecutive nucleotides of one of SEQ ID NOS. 1-6213, nucleic acids comprising nucleotide sequences which hybridize under moderate conditions to a nucleic acid complementary to one of SEQ ID NOS. 1-6213, nucleic acids comprising nucleotide sequences which hybridize under moderate conditions to a fragment comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides of the sequence complementary to one of SEQ ID  
35 NOS. 1-6213, nucleic acids comprising nucleotide sequences which hybridize under moderate conditions to a nucleic acid selected from the group consisting of SEQ ID NOS.: 6214-42397, nucleic acids comprising nucleic acid sequences which hybridize under moderate conditions to a fragment comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500

consecutive nucleotides of one of SEQ ID NOS.: 6214-42397, nucleic acids comprising nucleotide sequences which hybridize under moderate conditions to a nucleic acid complementary to one of SEQ ID NOS.: 6214-42397 and nucleic acids comprising nucleotide sequences which hybridize under moderate conditions to a fragment comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100,  
5 150, 200, 300, 400, or 500 consecutive nucleotides of the sequence complementary to one of SEQ ID NOS.: 6214-42397.

The homologous coding nucleic acids, homologous antisense nucleic acids or homologous polypeptides identified as above can then be used as targets or tools for the identification of new, antimicrobial compounds using methods such as those described herein. In some embodiments, the  
10 homologous coding nucleic acids, homologous antisense nucleic acids, or homologous polypeptides may be used to identify compounds with activity against more than one microorganism. [Placeholder]

For example, the preceding methods may be used to isolate homologous coding nucleic acids or homologous antisense nucleic acids comprising a nucleotide sequence with at least 97%, at least 95%, at least 90%, at least 85%, at least 80%, or at least 70% nucleotide sequence identity to a  
15 nucleotide sequence selected from the group consisting of one of the sequences of SEQ ID NOS. 1-6213, fragments comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides thereof, and the sequences complementary thereto. The preceding methods may also be used to isolate homologous coding nucleic acids or homologous antisense nucleic acids comprising a nucleotide sequence with at least 97%, at least 95%, at least 90%, at least 85%, at  
20 least 80%, or at least 70% nucleotide sequence identity to a nucleotide sequence selected from the group consisting of one of the nucleotide sequences of SEQ ID NOS.: 6214-42397, fragments comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides thereof, and the sequences complementary thereto. Identity may be measured using  
25 BLASTN version 2.0 with the default parameters. (Altschul, S.F. et al. Gapped BLAST and PSI-BLAST: A New Generation of Protein Database Search Programs, Nucleic Acid Res. 25: 3389-3402 (1997). For example, the homologous polynucleotides may comprise a coding sequence which is a naturally occurring allelic variant of one of the coding sequences described herein. Such allelic variants may have a substitution, deletion or addition of one or more nucleotides when compared to the nucleic acids of SEQ ID NOS.: 1-6213, SEQ ID NOS.: 6214-42397 or the  
30 nucleotide sequences complementary thereto.

Additionally, the above procedures may be used to isolate homologous coding nucleic acids which encode polypeptides having at least 99%, 95%, at least 90%, at least 85%, at least 80%, at least 70%, at least 60%, at least 50%, at least 40% or at least 25% amino acid identity or similarity to a polypeptide comprising the sequence of one of SEQ ID NOS.: 42398-78581 or to a polypeptide  
35 whose expression is inhibited by a nucleic acid of one of SEQ ID NOS.: 1-6213 or fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids thereof as determined using the FASTA version 3.0t78 algorithm with the default parameters. Alternatively, protein identity or similarity may be identified using BLASTP with the default



parameters, BLASTX with the default parameters, or TBLASTN with the default parameters. (Altschul, S.F. et al. Gapped BLAST and PSI-BLAST: A New Generation of Protein Database Search Programs, Nucleic Acid Res. 25: 3389-3402 (1997).

Alternatively, homologous coding nucleic acids, homologous antisense nucleic acids or homologous polypeptides may be identified by searching a database to identify sequences having a desired level of nucleotide or amino acid sequence homology to a nucleic acid or polypeptide involved in proliferation or an antisense nucleic acid to a nucleic acid involved in microbial proliferation. A variety of such databases are available to those skilled in the art, including GenBank and GenSeq. In some embodiments, the databases are screened to identify nucleic acids with at least 97%, at least 95%, at least 90%, at least 85%, at least 80%, or at least 70% nucleotide sequence identity to a nucleic acid required for proliferation, an antisense nucleic acid which inhibits proliferation, or a portion of a nucleic acid required for proliferation or a portion of an antisense nucleic acid which inhibits proliferation. For example, homologous coding sequences may be identified by using a database to identify nucleic acids homologous to one of SEQ ID Nos. 1-6213, homologous to fragments comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides thereof, nucleic acids homologous to one of SEQ ID NOS.: 6214-42397, homologous to fragments comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides of one of SEQ ID NOS.: 6214-42397, nucleic acids homologous to one of SEQ ID Nos. 1-6213, homologous to fragments comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides thereof or nucleic acids homologous to the sequences complementary to any of the preceding nucleic acids. In other embodiments, the databases are screened to identify polypeptides having at least 99%, 95%, at least 90%, at least 85%, at least 80%, at least 70%, at least 60%, at least 50%, at least 40% or at least 25% amino acid sequence identity or similarity to a polypeptide involved in proliferation or a portion thereof. For example, the database may be screened to identify polypeptides homologous to a polypeptide comprising one of SEQ ID NOs: 42398-78581, a polypeptide whose expression is inhibited by a nucleic acid of one of SEQ ID NOs: 1-6213 or homologous to fragments comprising at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids of any of the preceding polypeptides. In some embodiments, the database may be screened to identify homologous coding nucleic acids, homologous antisense nucleic acids or homologous polypeptides from cells or microorganisms other than the *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*,

*Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae* or *Yersinia pestis* species from which they were obtained. For example the database may be screened to identify homologous coding nucleic acids, homologous antisense nucleic acids or homologous polypeptides from microorganisms such as *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* or any species falling within the genera of any of the above species, including coagulase negative *Staphylococcus*. In some embodiments, the homologous coding nucleic acids, homologous antisense nucleic acids, or homologous polypeptides are from an organism other than *E. coli*.

In another embodiment, gene expression arrays and microarrays can be employed. Gene expression arrays are high density arrays of DNA samples deposited at specific locations on a glass chip, nylon membrane, or the like. Such arrays can be used by researchers to quantify relative gene expression under different conditions. Gene expression arrays are used by researchers to help identify optimal drug targets, profile new compounds, and determine disease pathways. An example of this technology is found in U.S. Patent No. 5,807,522.

It is possible to study the expression of all genes in the genome of a particular microbial organism using a single array. For example, the arrays may consist of 12 x 24 cm nylon filters containing PCR products corresponding to ORFs from *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*,  
 5 *Acinetobacter baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria*  
 10 *monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus*  
 15 *pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae* or *Yersinia pestis* (including the nucleic acids of SEQ ID NOs.: 6214-42397). 10 ngs of each PCR product are spotted every 1.5 mm on the filter. Single stranded labeled cDNAs are prepared for hybridization to the array (no second strand synthesis or amplification step is done) and placed in contact with the filter. Thus the labeled cDNAs are of "antisense" orientation.  
 20 Quantitative analysis is done by phosphorimager.

Hybridization of cDNA made from a sample of total cell mRNA to such an array followed by detection of binding by one or more of various techniques known to those in the art results in a signal at each location on the array to which cDNA hybridized. The intensity of the hybridization signal obtained at each location in the array thus reflects the amount of mRNA for that specific  
 25 gene that was present in the sample. Comparing the results obtained for mRNA isolated from cells grown under different conditions thus allows for a comparison of the relative amount of expression of each individual gene during growth under the different conditions.

Gene expression arrays may be used to analyze the total mRNA expression pattern at various time points after induction of an antisense nucleic acid complementary to a proliferation-  
 30 required gene. Analysis of the expression pattern indicated by hybridization to the array provides information on other genes whose expression is influenced by antisense expression. For example, if the antisense is complementary to a gene for ribosomal protein L7/L12 in the 50S subunit, levels of other mRNAs may be observed to increase, decrease or stay the same following expression of antisense to the L7/L12 gene. If the antisense is complementary to a different 50S subunit  
 35 ribosomal protein mRNA (e.g. L25), a different mRNA expression pattern may result. Thus, the mRNA expression pattern observed following expression of an antisense nucleic acid comprising a nucleotide sequence complementary to a proliferation required gene may identify other proliferation-required nucleic acids. In addition, the mRNA expression patterns observed when the

bacteria are exposed to candidate drug compounds or known antibiotics may be compared to those observed with antisense nucleic acids comprising a nucleotide sequence complementary to a proliferation-required nucleic acid. If the mRNA expression pattern observed with the candidate drug compound is similar to that observed with the antisense nucleic acid, the drug compound may be a promising therapeutic candidate. Thus, the assay would be useful in assisting in the selection of promising candidate drug compounds for use in drug development.

In cases where the source of nucleic acid deposited on the array and the source of the nucleic acid being hybridized to the array are from two different cells or microorganisms, gene expression arrays can identify homologous nucleic acids in the two cells or microorganisms.

The present invention also contemplates additional methods for screening other microorganisms for proliferation-required genes. In one aspect of this embodiment, an antisense nucleic acid comprising a nucleotide sequence complementary to the proliferation-required sequences from *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae* or *Yersinia pestis*, or a portion thereof, is transcribed in an antisense orientation in such a way as to alter the level or activity of a nucleic acid required for proliferation of an autologous or heterologous cell or microorganism. For example, the antisense nucleic acid may be a homologous antisense nucleic acid such as an antisense nucleic acid homologous to the nucleotide sequence complementary to one of SEQ ID NOs.: 6214-42397, an antisense nucleic acid comprising a nucleotide sequence homologous to one of SEQ ID Nos.: 1-6213, or an antisense nucleic acid comprising a nucleotide sequence complementary to a portion of any of the preceding nucleic acids. The cell or microorganism transcribing the homologous antisense nucleic acid may be used in a cell-based assay, such as those described herein, to identify candidate antibiotic compounds. In another embodiment, the conserved portions of nucleotide sequences identified as proliferation-required can be used to generate degenerate primers for use in the polymerase chain reaction (PCR). The PCR technique is well known in the art. The successful production of a PCR product using degenerate primers generated from the nucleotide sequences identified herein indicates the presence of a homologous gene sequence in the species being screened.

This homologous gene is then isolated, expressed, and used as a target for candidate antibiotic compounds. In another aspect of this embodiment, the homologous gene (for example a homologous coding nucleic acid) thus identified, or a portion thereof, is transcribed in an autologous cell or microorganism or in a heterologous cell or microorganism in an antisense orientation in such a way as to alter the level or activity of a homologous gene required for proliferation in the autologous or heterologous cell or microorganism. Alternatively, a homologous antisense nucleic acid may be transcribed in an autologous or heterologous cell or microorganism in such a way as to alter the level or activity of a gene product required for proliferation in the autologous or heterologous cell or microorganism.

The nucleic acids homologous to the genes required for the proliferation of *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae* or *Yersinia pestis* or the sequences complementary thereto may be used to identify homologous coding nucleic acids or homologous antisense nucleic acids from cells or microorganisms other than *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae* or *Yersinia pestis* to inhibit the proliferation of cells or microorganisms other than

*Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*,  
*Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter baumannii*, *Bacillus anthracis*,  
*Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*,  
*Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*,  
5 *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*,  
*Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus faecium*, *Haemophilus*  
*influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella*  
*catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium*  
*tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria*  
10 *meningitidis*, *Pasteurella multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas*  
*syringae*, *Salmonella paratyphi*, *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus*  
*haemolyticus*, *Streptococcus mutans*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*,  
*Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae* or *Yersinia pestis* by inhibiting the  
activity or reducing the amount of the identified homologous coding nucleic acid or homologous  
15 polypeptide in the cell or microorganism other than *Escherichia coli*, *Staphylococcus aureus*,  
*Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*,  
*Acinetobacter baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia*  
*burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter*  
*jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium*  
20 *botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus*  
*faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria*  
*monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*,  
*Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma*  
*pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus*  
25 *mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*,  
*Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus*  
*pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio*  
*cholerae* or *Yersinia pestis* or to identify compounds which inhibit the growth of cells or  
microorganisms other than *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*,  
30 *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter*  
*baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*,  
*Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*,  
*Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium*  
*botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus*  
35 *faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria*  
*monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*,  
*Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma*  
*pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus*

*mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*,  
*Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus*  
*pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio*  
*cholerae* or *Yersinia pestis* as described below. For example, the nucleic acids homologous to  
5 proliferation-required genes from *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*,  
*Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter*  
*baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*,  
*Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*,  
*Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium*  
10 *botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus*  
*faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria*  
*monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*,  
*Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma*  
*pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus*  
15 *mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*,  
*Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus*  
*pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio*  
*cholerae* or *Yersinia pestis* or the sequences complementary thereto may be used to identify  
compounds which inhibit the growth of *Acinetobacter baumannii*, *Anaplasma marginale*,  
20 *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia*  
*burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter*  
*jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*,  
*Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida*  
*pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*,  
25 *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*,  
*Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter*  
*cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*,  
*Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*,  
*Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*,  
30 *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma*  
*pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella*  
*haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*,  
*Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*,  
*Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella*  
35 *typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*,  
*Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus*  
*pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma*  
*urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*,

*Yersinia pestis* or any species falling within the genera of any of the above species. In some embodiments of the present invention, the nucleic acids homologous to proliferation-required sequences from *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter baumannii*,  
 5 *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria monocytogenes*,  
 10 *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus pneumoniae*,  
 15 *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae* or *Yersinia pestis* (including nucleic acids homologous to one of SEQ ID NOs.: 6214-42397) or the sequences complementary thereto (including nucleic acids homologous to one of SEQ ID NOs.: 1-6213) are used to identify proliferation-required sequences in an organism other than *E. coli*.

In another embodiment of the present invention, antisense nucleic acids complementary to the  
 20 sequences identified as required for proliferation or portions thereof (including antisense nucleic acids comprising a nucleotide sequence complementary to one of SEQ ID NOs.: 6214-42397 or portions thereof, such as the nucleic acids of SEQ ID NOs.: 1-6213) are transferred to vectors capable of function within a species other than the species from which the sequences were obtained. For example, the vector may be functional in *Acinetobacter baumannii*, *Anaplasma marginale*,  
 25 *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*,  
 30 *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*,  
 35 *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*,



*Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* or any species falling within the genera of any of the above species. In some embodiments of the present invention, the vector may be functional in an organism other than *E. coli*. As would be appreciated by one of ordinary skill in the art, vectors may contain certain elements that are species specific. These elements can include promoter sequences, operator sequences, repressor genes, origins of replication, ribosomal binding sequences, termination sequences, and others. To use the antisense nucleic acids, one of ordinary skill in the art would know to use standard molecular biology techniques to isolate vectors containing the sequences of interest from cultured bacterial cells, isolate and purify those sequences, and subclone those sequences into a vector adapted for use in the species of bacteria to be screened.

Vectors for a variety of other species are known in the art. For example, numerous vectors which function in *E. coli* are known in the art. Also, Pla et al. have reported an expression vector that is functional in a number of relevant hosts including: *Salmonella typhimurium*, *Pseudomonas putida*, and *Pseudomonas aeruginosa*. *J. Bacteriol.* 172(8):4448-55 (1990). Brunschwig and Darzins (Gene (1992) 111:35-4, described a shuttle expression vector for *Pseudomonas aeruginosa*. Vectors useful for the production of stabilized mRNA having an increased lifetime (including antisense RNA) in Gram negative organisms are described in U.S. Provisional Patent Application Serial Number 60/343,512, filed December 21, 2001. Similarly many examples exist of expression vectors that are freely transferable among various Gram positive microorganisms. Expression vectors for *Enterococcus faecalis* may be engineered by incorporating suitable promoters into a pAK80 backbone (Israelsen, H., S. M. Madsen, A. Vrang, E. B. Hansen and E. Johansen. 1995. *Appl. Environ. Microbiol.* 61:2540-2547. A number of vectors useful for nucleic acid expression (including antisense nucleic acid expression) in *Enterococcus faecalis*, *Staphylococcus aureus* as well as other Gram positive organisms are described in U.S. Patent Application Serial Number 10/032,393, filed December 21, 2001.

Following the subcloning of the antisense nucleic acids complementary to proliferation-required sequences from *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*,

*Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae* or *Yersinia pestis* or portions thereof into a vector functional in a second cell or microorganism of interest (i.e. a cell or microorganism other than the one from which the identified nucleic acids were obtained), the antisense nucleic acids are conditionally transcribed to test for bacterial growth inhibition. The nucleotide sequences of the nucleic acids from *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae* or *Yersinia pestis* that, when transcribed, inhibit growth of the second cell or microorganism are compared to the known genomic sequence of the second cell or microorganism to identify the homologous gene from the second organism. If the homologous sequence from the second cell or microorganism is not known, it may be identified and isolated by hybridization to the proliferation-required *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio*

*cholerae* or *Yersinia pestis* sequence of interest or by amplification using PCR primers based on the proliferation-required nucleotide sequence of interest as described above. In this way, sequences which may be required for the proliferation of the second cell or microorganism may be identified. For example, the second microorganism may be *Acinetobacter baumannii*, *Anaplasma marginale*,  
 5 *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*,  
 10 *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*,  
 15 *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*,  
 20 *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* or any species falling within the genera of any of the above species. In some  
 25 embodiments of the present invention, the second microorganism is an organism other than *E. coli*.

The homologous nucleic acid sequences from the second cell or microorganism which are identified as described above may then be operably linked to a promoter, such as an inducible promoter, in an antisense orientation and introduced into the second cell or microorganism. The techniques described herein for identifying *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus*  
 30 *faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus*  
 35 *faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus*

*mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae* or *Yersinia pestis* genes required for proliferation may thus be employed to determine whether the identified nucleotide sequences from a second cell or microorganism inhibit the proliferation of the second cell or microorganism. For example, the second microorganism may be *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* or any species falling within the genera of any of the above species. In some embodiments of the present invention, the second microorganism may be an organism other than *E. coli*.

Antisense nucleic acids required for the proliferation of microorganisms other than *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium*

*tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*,  
5 *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae* or *Yersinia pestis* or the genes corresponding thereto, may also be hybridized to a microarray containing the *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*,  
10 *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium diptheriae*, *Enterobacter cloacae*, *Enterococcus faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae* or *Yersinia pestis* (including the nucleic acids of SEQ ID NOs.: 6214-  
20 42397) to gauge the homology between the *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium diptheriae*, *Enterobacter cloacae*, *Enterococcus faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*,  
30 *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae* or *Yersinia pestis* sequences and the proliferation-required nucleic acids from other cells or microorganisms. For example, the proliferation-required nucleic acid may be from  
35 *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida*

*guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*,  
 5 *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*,  
 10 *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* or any species falling within the genera of any of the above species. In some embodiments of the present invention, the proliferation-required nucleotide sequences from  
*Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*,  
 20 *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus*  
 25 *haemolyticus*, *Streptococcus mutans*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae* or *Yersinia pestis* or homologous nucleic acids are used to identify proliferation-required sequences in an organism other than *E. coli*. In some embodiments of the present invention, the proliferation-required sequences may be from an organism other than *E. coli*. The proliferation-required nucleic acids from a cell or microorganism  
 30 other than *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*,

*Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae* or *Yersinia pestis* may be hybridized to the array under a variety of conditions which permit hybridization to occur when the probe has different levels of homology to the nucleotide sequence on the microarray. This would provide an indication of homology across the cells or microorganisms as well as clues to other possible essential genes in these cells or microorganisms.

In some embodiments of the present invention, the essential gene products described herein are used in methods of identifying a target on which a compound that inhibits cellular proliferation acts. Such methods are described in the U.S. Patent Application entitled METHODS FOR IDENTIFYING THE TARGET OF A COMPOUND WHICH INHIBITS CELLULAR PROLIFERATION, filed February 8, 2002. As employed herein, some embodiments of methods used to identify a target on which a compound that inhibits cellular proliferation acts utilize collections or cultures of strains comprising strains which either overexpress a different gene product which is required for cellular proliferation (such as the gene products described herein) or underexpress a different gene product (such as the gene products described herein) which is required for cellular proliferation (i.e. at least some of the strains in the culture overexpress or underexpress a gene product required for cellular proliferation). In some embodiments, the present invention uses collections or cultures of strains comprising both strains which overexpress gene products required for cellular proliferation and strains which underexpress the same gene products required for cellular proliferation. Preferably, each of the strains present in the culture or collection either overexpresses or underexpresses a different gene product which is required for cellular proliferation (i.e. all of the strains in the culture overexpress or underexpress a gene product required for cellular proliferation). However, in some embodiments, the culture or collection may include one or more strains which do not overexpress or underexpress a gene product which is required for proliferation. The gene product which is overexpressed or underexpressed in each strain may be any gene product which is required for cellular proliferation, including a gene product whose activity or level is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 6214-42397, a gene product comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42398-78581, a gene product whose activity or level is inhibited by a homologous

antisense nucleic acid, a gene product encoded by a homologous coding nucleic acid, and a gene product comprising a homologous polypeptide.

As used herein the term "culture" refers to a plurality of strains growing in a single aliquot of a liquid growth medium and the term "collection" refers to a plurality of strains each of which is growing in a separate aliquot of liquid growth medium or a different location on a solid growth medium.

In some embodiments, if desired, one or more of the strains in the culture or collection of strains may overexpress or underexpress more than one gene product described herein which is required for cellular proliferation. In this embodiment, the gene products which are overexpressed or underexpressed in one or more of the strains may be functionally related or functionally unrelated. This may facilitate the identification of compounds when two or more gene products share similar functions in the cell or where the cell has multiple biochemical pathways which lead to a particular end product.

Alternatively, if the gene product described herein to be overexpressed or underexpressed is encoded by a gene which is part of an operon containing a plurality of genes, the desired gene may be overexpressed or underexpressed while the remaining genes in the operon are expressed at levels where they do not impact the ability of the cell to grow in the presence of a particular compound. For example, the desired gene may be placed under the control of a regulatable promoter, a transcriptional terminator may be placed 3' of the desired gene and a promoter, preferably a constitutive promoter, may be placed 3' of the transcriptional terminator and 5' of the remaining genes in the operon.

In some embodiments, the culture or collection of strains may comprise a strain which overexpresses or underexpresses a gene product whose activity or level is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 1-6213.

In some embodiments, the culture or collection of strains may comprise strains which in aggregate overexpress or underexpress at least two gene products whose activity or level is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOS.: 1-6213, at least 10 gene products whose activity or level is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOS.: 1-6213, at least 20 gene products whose activity or level is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOS.: 1-6213, at least 30 gene products whose activity or level is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOS.: 1-6213, at least 50 gene products whose activity or level is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOS.: 1-6213, at least 100 gene products whose activity or level is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOS.: 1-6213, at least 300 gene products whose activity or level is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOS.: 1-6213 or more than 300 gene products whose activity or level is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOS.: 1-6213, wherein each strain in the culture or collection of strains overexpresses or underexpresses a single gene



product whose activity or level is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOs. 1-6213. Alternatively, if desired, one or more of the strains in the culture or collection of strains may overexpress or underexpress more than one gene product whose activity or level is inhibited by a nucleic acid selected from the group consisting of SEQ ID NOs. 1-6213.

5 In other embodiments, the culture or collection of strains may comprise a strain which overexpresses or underexpresses a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 6214-42397. In some embodiments, the culture or collection of strains may comprise strains which in aggregate overexpress or underexpress at least two gene products encoded by a nucleic acid comprising a nucleotide  
10 sequence selected from the group consisting of SEQ ID NOs.: 6214-42397, at least 10 gene products encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 6214-42397, at least 20 gene products encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 6214-42397, at least 30 gene products encoded by a nucleic acid comprising a nucleotide sequence selected from  
15 the group consisting of SEQ ID NOs.: 6214-42397, at least 50 gene products encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 6214-42397, at least 100 gene products encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 6214-42397, at least 300 gene products encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of  
20 SEQ ID NOs.: 6214-42397 or more than 300 gene products encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 6214-42397, wherein each strain in the culture or collection of strains overexpresses or underexpresses a single gene product encoded by a nucleic acid selected from the group consisting of SEQ ID NOs. 6214-42397. Alternatively, if desired, one or more strains in the culture or collection of strains may overexpress  
25 or underexpress more than one gene product encoded by a nucleic acid selected from the group consisting of SEQ ID NOs. 6214-42397.

In some embodiments the culture or collection of strains comprises a strain in which a gene product comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42938-78581 is overexpressed or underexpressed. In some embodiments, the culture or collection  
30 of strains may comprise strains which in aggregate overexpress or underexpress at least two gene products comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42938-78581, at least 10 gene products comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42938-78581, at least 20 gene products comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42938-78581, at least 30 gene  
35 products comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42938-78581, at least 50 gene products comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42938-78581, at least 100 gene products comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42938-78581, at least 300 gene

products comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42938-78581 or more than 300 gene products comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42938-78581, wherein each strain in the culture or collection of strains overexpresses or underexpresses a single gene product selected from the group consisting of SEQ ID NOs. 42938-78581. Alternatively, if desired one or more of the strains in the culture or collection of strains may overexpress or underexpress more than one gene product selected from the group consisting of SEQ ID NOs. 42938-78581.

In other embodiments, the culture or collection of strains comprises a strain in which at least one of the gene products encoded by a homologous coding nucleic acid as defined above is overexpressed or underexpressed. In some embodiments, the culture or collection of strains may comprise strains which in aggregate overexpress or underexpress at least 2, at least 10, at least 20, at least 30, at least 50, at least 100, at least 300 or more than 300 gene products encoded by a homologous coding nucleic acid as defined above. If desired the culture or collection of strains may comprise one or more strains which overexpress or underexpress more than one gene product encoded by a homologous coding nucleic acid. In further embodiments, the culture or collection of strains comprises a strain in which at least one, at least 10, at least 20, at least 30, at least 50, at least 100, at least 300 or more than 300 homologous polypeptides as defined above is overexpressed or underexpressed. If desired the culture or collection of strains may comprise one or more strains which overexpress or underexpress more than one homologous polypeptide.

For example, in some embodiments, the culture or collection of strains comprises a strain in which at least one gene product selected from the group consisting of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 under stringent conditions, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 is overexpressed or underexpressed, wherein each strain overexpresses or underexpresses one gene product. In some

embodiments, the culture or collection of strains may comprise strains in which in aggregate at least 2, at least 10, at least 20, at least 30, at least 50, at least 100, at least 300, or more than 300 gene products selected from the group consisting of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 under stringent conditions, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 is overexpressed or underexpressed, wherein each strain overexpresses or underexpresses one gene product.

If desired, one or more of the strains in the culture or collection of strains may overexpress or underexpress more than one gene product selected from the group consisting of a gene product having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleic acid encoding a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product having at least 25% amino acid identity as determined using FASTA version 3.0t78 with the default parameters to a gene product whose expression is inhibited by an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 under stringent conditions, a gene product encoded by a nucleic acid which hybridizes to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213 under moderate conditions, and a gene product whose activity may be complemented by the gene product whose activity is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213.

In further embodiments, the culture or collection of strains comprises a strain in which at least one gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of a nucleic acid comprising a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397, a nucleic acid comprising a nucleotide sequence which hybridizes to a sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under stringent conditions, and a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under moderate conditions is overexpressed or underexpressed, wherein each strain overexpresses or underexpresses one gene product. In some embodiments, the culture or collection of strains comprises a strain or a group of strains in which in aggregate at least 2, at least 10, at least 20, at least 30, at least 50, at least 100, at least 300, or more than 300 gene products encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of a nucleic acid comprising a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397, a nucleic acid comprising a nucleotide sequence which hybridizes to a sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under stringent conditions, and a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under moderate conditions is overexpressed or underexpressed, wherein each strain overexpresses or underexpresses one gene product.

If desired, one or more of the strains in the culture or collection of strains may overexpress or underexpress more than one gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of a nucleic acid comprising a nucleic acid having at least 70% nucleotide sequence identity as determined using BLASTN version 2.0 with the default parameters to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397, a nucleic acid comprising a nucleotide sequence which hybridizes to a sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under stringent conditions, and a nucleic acid comprising a nucleotide sequence which hybridizes to a nucleotide sequence selected from the group consisting of SEQ ID NOS.: 6214-42397 under moderate conditions.

In additional embodiments, the culture or collection of strains comprises a strain in which at least one gene product comprising a polypeptide selected from the group consisting of a polypeptide having at least 25% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide selected from the group consisting of SEQ ID NOS.: 42938-78581 and a polypeptide whose activity may be complemented by a polypeptide selected from the group consisting of SEQ ID NOS.: 42938-78581 is overexpressed or underexpressed, wherein each strain overexpresses or underexpresses one gene product. In some embodiments, the culture or collection of strains comprises a strain or a group of strains in which in aggregate at least 2, at least 10, at least 20, at

least 30, at least 50, at least 100, at least 300, or more than 300 gene products comprising a polypeptide selected from the group consisting of a polypeptide having at least 25% amino acid identity as determined using FASTA version 3.0t78 to a polypeptide selected from the group consisting of SEQ ID NOs: 42938-78581 and a polypeptide whose activity may be complemented  
 5 by a polypeptide selected from the group consisting of SEQ ID NOs: 42938-78581 is overexpressed or underexpressed, wherein each strain overexpresses or underexpresses one gene product.

If desired, one or more of the strains in the culture or collection of strains may overexpress or underexpress more than one polypeptide selected from the group consisting of a polypeptide having at least 25% amino acid identity as determined using FASTA version 3.0t78 to a  
 10 polypeptide selected from the group consisting of SEQ ID NOs: 42938-78581 and a polypeptide whose activity may be complemented by a polypeptide selected from the group consisting of SEQ ID NOs: 42938-78581.

The methods of the present invention may be used to identify the targets of compounds which inhibit the proliferation of any desired cell or organism. In some embodiments, these  
 15 methods are employed to identify the targets of compounds which inhibit the proliferation of bacteria, fungi, or protozoans. In further embodiments, these methods are employed to identify the targets of compounds which inhibit the growth of an organism selected from the group consisting of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*,  
 20 *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*,  
 25 *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*,  
 30 *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*,  
 35 *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* or any species falling within the genera of any of the above species.

Overexpression may be obtained using a variety of techniques familiar to those skilled in the art. For example, overexpression may be obtained by operably linking a gene encoding a gene product whose activity or level is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 6214-42397, a gene product comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42398-78581, a gene product whose activity or level is inhibited by a homologous antisense nucleic acid, a gene product encoded by a homologous coding nucleic acid, or a gene product comprising a homologous polypeptide to a promoter which transcribes a higher level of mRNA encoding or comprising the gene product than does a wild type cell.

A variety of promoters may be used to overexpress the gene product described herein, including a gene product whose activity or level is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 6214-42397, a gene product comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42398-78581, a gene product whose activity or level is inhibited by a homologous antisense nucleic acid, a gene product encoded by a homologous coding nucleic acid, and a gene product comprising a homologous polypeptide. The promoters used to overexpress the gene product may be relatively strong promoters, promoters which possess a moderate level of activity, or relatively weak promoters and may be either constitutive or regulatable promoters. In some embodiments, several strains, each of which overexpresses the gene product to a different extent, may be used in order to optimize the degree of overexpression of the gene product.

In some embodiments, each of the gene products required for proliferation may be placed under the control of several different promoters of varying strengths to create several different strains which express the gene product at varying levels. The level of expression of the gene product in each of the strains is compared to that in wild type cells in order to identify a promoter which provides a desired level of expression relative to wild type cells (i.e. a desired level of overexpression or underexpression). The strain having the desired level of expression is then included in a culture or collection of strains to be contacted with a test compound as discussed below. Examples of suites of regulatable promoters having varying strengths that are useful for the expression of gene products at varying levels are described in U.S. Patent Application Serial Number 10/032,393, filed on December 21, 2002.

The promoter is selected to be active in the type of cell in which the gene product is to be expressed. For example, for overexpression of the gene product in mammalian cells, the gene encoding the gene product may be operably linked to promoters such as the SV40 promoter, the metallothionein promoter, the MMTV promoter, the RSV promoter, the tetP promoter, the adenovirus major late promoter or other promoters known to those skilled in the art. In yeast, the gene encoding the gene product may be operably linked to promoters such as the CYC1, ADHI,

ADHIII, GAL1, GAL10, PHO5, PGK or other promoters used in the art. Similarly, in bacteria, the gene encoding the gene product may be operably linked to the , SP6, T3, trc promoter, lac promoter, temperature regulated lambda promoters, the *Bacillus* aprE and nprE promoters (U.S. Patent No. 5,387,521), the bacteriophage lambda P<sub>L</sub> and P<sub>R</sub> promoters (Renaut, et al., (1981) Gene 15: 81) the trp promoter (Russell, et al., (1982) Gene 20: 23), the tac promoter (de Boer et al., (1983) Proc. Natl. Acad. Sci. USA 80: 21), *B. subtilis* alkaline protease promoter (Stahl et al., (1984) J. Bacteriol. 158, 411-418) alpha amylase promoter of *B. subtilis* (Yang et al., (1983) Nucleic Acids Res. 11, 237-249) or *B. amyloliquefaciens* (Tarkinen, et al, (1983) J. Biol. Chem. 258, 1007-1013), the neutral protease promoter from *B. subtilis* (Yang et al, (1984) J. Bacteriol. 160, 15-21), T7 RNA polymerase promoter (Studier and Moffatt (1986) J Mol Biol. 189(1):113-30), *B. subtilis* xyl promoter or mutant tetR promoter active in bacilli (Geissendorfer & Hillen (1990) Appl. Microbiol. Biotechnol. 33:657-663), Staphylococcal enterotoxin D promoter (Zhang and Stewart (2000) J. Bacteriol. 182(8):2321-5), cap8 operon promoter from *Staphylococcus aureus* (Ouyang et al., (1999) J. Bacteriol. 181(8):2492-500), the lactococcal nisA promoter (Eichenbaum (1998) Appl Environ Microbiol. 64(8):2763-9), promoters from in *Acholeplasma laidlawii* (Jarhede et al., (1995) Microbiology 141 ( Pt 9):2071-9), porA promoter of *Neisseria meningitidis* (Sawaya et al., (1999) Gene 233:49-57), the fbpA promoter of *Neisseria gonorrhoeae* (Forng et al., (1997) J. Bacteriol. 179:3047-3052), *Corynebacterium diphtheriae* toxin gene promoter (Schmitt and Holmes (1994) J. Bacteriol. 176(4):1141-9), the hasA operon promoter from Group A Streptococci (Alberti et al., (1998) Mol Microbiol 28(2):343-53), the rpoS promoter of *Pseudomonas putida* (Kojic and Venturi (2001) J. Bacteriol. 183:3712-3720), the *Acinetobacter baumannii* phosphate regulated *ppk* gene promoter (Gavigan et al., Microbiology 145:2931-7 (1999)); the *Acinetobacter baumannii* *adhC1* promoter which is induced under iron limitation and repressed when the cells are cultured in the presence of free inorganic iron (Echenique et al., Microbiology 147:2805-15 (2001)); the *flaB* promoter of pGK12 active in *Borrelia burgdorferi* (Sartakova et al., Proc Natl Acad Sci U S A. 97(9):4850-5 (2000)); the use of P<sub>trc</sub> promoter results in strong inducer-dependent expression in *Burkholderia spp* (Santos et al., FEMS Microbiol Lett 195(1):91-6 (2001)); the iron regulated *sodA* promoter of *Bordetella pertussis* (Graeff-Wohlleben et al., J Bacteriol 179(7):2194-201 (1997)); UV-inducible *bcn* and *uviAB* promoters in *Clostridia spp* (Garnier and Cole Mol Microbiol 2(5):607-14 (1988)); the heat-inducible *clpB* promoter of *Campylobacter jejuni* (Thies et al., Gene 230(1):61-7 (1999)); promoters carrying bacteriophage C1 operator sites in *Klebsiella pneumoniae* (Schoefield et al, J Bacteriol 183(23):6947-50 (2001)); the *Proteus mirabilis* *ureR* promoter (Poore et al., J Bacteriol 183(15):4526-35 (2001)); and the heat-inducible *groESL* promoter in *Listeria monocytogenes*, and the IPTG inducible promoter in pLEX5BA (Krause et al., J. Mol. Biol. 274: 365 (1997). In another embodiment, which may be useful in *Staphylococcus aureus*, the promoter is a novel inducible promoter system, XylT5, comprising a modified T5 promoter fused to the *xylO* operator from the *xylA* promoter of *Staphylococcus aureus*. This promoter is described in U.S. Patent Application Serial Number 10/032,393. In another embodiment the promoter may be a two-

component inducible promoter system in which the T7 RNA polymerase gene is integrated on the chromosome and is regulated by *lacUV5/ lacO* (Brunschwig, E. and Darzins, A. 1992. Gene 111:35-41, and a T7 gene 10 promoter, which is transcribed by T7 RNA polymerase, is fused with a *lacO* operator. In another embodiment the promoter may be the promoters from the plasmids pEPEF3 or pEPEF14, which harbor xylose inducible promoters functional in *E. faecalis*, described in U.S. Patent Application Serial No. 10/032,393. Other promoters which may be used are familiar to those skilled in the art. In fungi, the gene encoding the gene product may be operably linked to the CaACT1 promoter (Morschhauser, Mol. Gen. Genet. 257: 412-420 (1998), or other promoters familiar to those skilled in the art. It will be appreciated that other combinations of organisms and promoters may also be used in the present invention.

In some embodiments, overexpression may be achieved by using homologous recombination to replace the natural promoter which drives expression of the proliferation-required genes described herein with a regulatable promoter. For example, the methods described in U.S. Patent Application 09/948,993 may be used to place the gene required for proliferation under the control of a regulatable promoter. Examples of gene products, which are encoded by genes that can be overexpressed by regulatable promoters introduced by such promoter replacement methods include a gene product whose activity or level is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 6214-42397, a gene product comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42398-78581, a gene product whose activity or level is inhibited by a homologous antisense nucleic acid, a gene product encoded by a homologous coding nucleic acid, and a gene product comprising a homologous polypeptide.

Briefly, in some embodiments of these methods in which natural promoters are replaced by regulatable promoters, the cells may be haploid, such as bacterial cells. Regulatable promoters that are useful for promoter replacement in bacterial cells include, but are not limited to, the promoters described in U.S. Patent Application Serial Number 10/032,393 filed December 21, 2001. A linear promoter replacement cassette comprising a regulatable promoter flanked by nucleotide sequences having homology to the natural promoter is introduced into the cell. In some embodiments, the cassette also comprises a nucleotide sequence encoding a selectable marker or a marker whose expression is readily identified. The cassette may be a double stranded nucleic acid or a single stranded nucleic acid as described in U.S. Patent Application Serial Number 09/948,993. Upon homologous recombination, the natural promoter is replaced with the regulatable promoter, leaving the gene required for proliferation under the control of the regulatable promoter. Strains in which the gene required for proliferation is under control of the regulatable promoter are grown under conditions in which the regulatable promoter provides a level of the proliferation-required gene product which is above the level in a wild type cell. For example, the strains may be grown in the



presence of an inducer which induces expression from the regulatable promoter, or under conditions in which the action of a repressor on the regulatable promoter is reduced or eliminated.

Alternatively, rather than replacing the native promoters of each of the genes encoding a proliferation-required gene product described herein with a single desired replacement promoter, a plurality of replacement promoters which provide desired expression levels for the gene products to be overexpressed or underexpressed are used. The method is performed as described above except that rather than using a single labeled primer complementary to a nucleotide sequence within the single replacement promoter, a plurality of labeled primers complementary to suitable nucleotide sequences in the plurality of replacement promoters are used.

Alternatively, in embodiments in which the level or activity of proliferation-required gene products described herein is reduced by transcribing an antisense nucleic acid complementary to at least a portion of the genes encoding such gene products, the strains may be designed such that the length of the nucleotide sequence encoding the antisense nucleic acid is different for each gene. Amplification reactions are performed as described above using primers at each end of the gene encoding the antisense nucleic acid such that the amplification product corresponding to each gene has a unique length or a dye which allows it to be distinguished from other amplification products of the same length. Alternatively, the lengths of the nucleotide sequences encoding the antisense nucleic acids may not be unique for each gene, but the primers used in the amplification reaction may be selected such that the length of the amplification product corresponding to each gene is unique.

In another embodiment, the native promoters may be replaced with promoters which include therein or adjacent thereto a unique nucleotide sequence which is distinct from that present in the other replacement promoters in the strains in the culture or collection of strains. In this embodiment, each promoter includes or has adjacent thereto a unique "tag" which may be used to identify strains which proliferate more rapidly or more slowly in the culture or collection of strains. The tag may be detected using hybridization based methods or amplification based methods, including the amplification method which generates amplification products having a unique size for each proliferation required gene described above.

Alternatively, the native promoter which directs the transcription of the proliferation-required genes described herein may rendered regulatable by inserting a regulatory element into the chromosome of the cell via homologous recombination such that the regulatory element regulates the level of transcription from the promoter. Examples of gene products, which are encoded by genes that have promoters which can be rendered regulatable by regulatory elements inserted by such methods include a gene product whose activity or level is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 6214-42397, a gene product comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42398-78581, a gene product whose activity or

level is inhibited by a homologous antisense nucleic acid, a gene product encoded by a homologous coding nucleic acid, and a gene product comprising a homologous polypeptide.

A variety of regulatory elements may be used to regulate the expression of essential gene products described herein. The regulatory element may be an operator which is recognized by a repressor (e.g. lac, tet, araBAD repressors) or a nucleotide sequence which is recognized by a transcriptional activator. In some embodiments, the regulatory element may be a transcriptional terminator, a nucleotide sequence which introduces a bend in the DNA or an upstream activating sequence. A linear regulatory element insertion cassette comprising a regulatory element flanked by nucleotide sequences having homology to the natural promoter is introduced into the cell. In some embodiments, the cassette also comprises a nucleotide sequence encoding a selectable marker or a marker whose expression is readily identified. The cassette may be a double stranded nucleic acid or a single stranded nucleic acid as described in U.S. Patent Application Serial Number 09/948,993. Upon homologous recombination, the regulatory element is inserted into the chromosome, leaving the gene required for proliferation under the control of the regulatory element. Strains in which the gene required for proliferation is under control of the regulatory element are grown under conditions in which the regulatable promoter provides a level of the proliferation-required gene product which is above the level in a wild type cell. For example, the strains may be grown in the presence of an inducer which induces expression from the promoter, or under conditions in which the action of a repressor on the promoter is reduced or eliminated. It will be appreciated that the amplification method which generates amplification products having a unique size for each proliferation required gene may be used to detect strains which are overrepresented or underrepresented in the culture or collection of strains. For example, if desired, primers complementary to a nucleotide sequence within the regulatory element may be used in the amplification reaction.

The promoter replacement cassette or regulatory element insertion cassette may be a double stranded nucleic acid, such as an amplicon generated through PCR or other amplification methods, or a single stranded nucleic acid, such as an oligonucleotide. For example, single stranded nucleic acids may be introduced into the chromosome using the methods described in Ellis et al., PNAS 98: 6742-6746, 2001.

In some embodiments, the cell into which the promoter replacement cassette or regulatory element insertion cassette is introduced has an enhanced frequency of recombination. For example, the cells may lack or have a reduced level or activity of one or more exonucleases which would ordinarily degrade the DNA to be inserted into the chromosome. In further embodiments, the cells may both lack or have reduced levels of exonucleases and express or overexpress proteins involved in mediating homologous recombination. For example, if the methods are performed in *Escherichia coli* or other enteric prokaryotes, cells in which the activity of exonuclease V of the RecBCD recombination pathway, which degrades linear nucleic acids, has been reduced or eliminated, such as recB, recC, or recD mutants may be used. In some embodiments, the cells have

mutations in more than one of the *recB*, *recC*, and *recD* genes which enhance the frequency of homologous recombination. For example the cells may have mutations in both the *recB* and *recC* genes.

The promoter replacement or regulatory element insertion methods may also be performed in *Escherichia coli* cells in which the activity of the RecET recombinase system of the Rac prophage has been activated, such as cells which carry an *sbcA* mutation. The *RecE* gene of the rac prophage encodes ExoVIII a 5'-3' exonuclease, while the *RecT* gene of the Rac prophage encodes a single stranded DNA binding protein which facilitates renaturation and D-loop formation. Thus, the gene products of the *RecE* and *RecT* genes or proteins with analogous functions facilitate homologous recombination. The *RecE* and *RecT* genes lie in the same operon but are normally not expressed. However, *sbcA* mutants activate the expression the *RecE* and *RecT* genes. In some embodiments, the methods may be performed in cells which carry mutations in the *recB* and *recC* genes as well as the *sbcA* mutation. The *RecE* and *RecT* gene may be constitutively or conditionally expressed. For example, the methods may be performed in *E. coli* strain JC8679, which carries the *sbcA23*, *recB21* and *recC22* mutations.

In some embodiments, the methods may be performed in *Escherichia coli* cells in which recombination via the *RecF* pathway has been enhanced, such as cells which carry an *sbcB* mutation.

It will be appreciated that the *RecE* and *RecT* gene products, or proteins with analogous functions may be conditionally or constitutively expressed in prokaryotic organisms other than *E. coli*. In some embodiments, these proteins may be conditionally or constitutively expressed in *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*,

*Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* or any species falling within the genera of any of the above species. For example, plasmids encoding these gene products may be introduced into the organism. If desired, the coding sequences encoding these gene products may be optimized to reflect the codon preferences of the organism in which they are to be expressed. Similarly, in some embodiments, the organism may contain mutations analogous to the *recB*, *recC*, *recD*, *sbcA* or *sbcB* mutations which enhance the frequency of homologous recombination.

In further embodiments, the promoter replacement or regulatory element insertion methods may be conducted in cells which utilize the Red system of bacteriophage lambda ( $\lambda$ ) or analogous systems from other phages to enhance the frequency of homologous recombination. The Red system contains three genes, ( $\gamma$ ,  $\beta$  and *exo* whose products are the Gam, Bet and Exo proteins (see Ellis et al. PNAS 98:6742-6746, 2001. The Gam protein inhibits the RecBCD exonuclease V, thus permitting Beta and Exo to gain access to the ends of the DNA to be integrated and facilitating homologous recombination. The Beta protein is a single stranded DNA binding protein that promotes the annealing of a single stranded nucleic acid to a complementary single stranded nucleic acid and mediates strand exchange. The Exo protein is a double-stranded DNA dependent 5'-3' exonuclease that leaves 3' overhangs that can act as substrates for recombination. Thus, constitutive or conditional expression of the  $\lambda$  Red proteins or proteins having analogous functions facilitates homologous recombination.

It will be appreciated that the  $\lambda$  Beta, Gam and Exo proteins, or proteins with analogous functions may be expressed constitutively or conditionally in prokaryotic organisms other than *E. coli*. In some embodiments, these proteins may be conditionally or constitutively expressed in *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*,

*Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* or any species falling within the genera of any of the above species. For example, plasmids encoding these gene products may be introduced into the organism. If desired, the coding sequences encoding these gene products may be optimized to reflect the codon preferences of the organism in which they are to be expressed.

In some embodiments, the cells may have an increased frequency of homologous recombination as a result of more than one of the aforementioned characteristics. In some embodiments, the enhanced frequency of recombination may be a conditional characteristic of the cells which depends on the culture conditions in which the cells are grown. For example, in some embodiments, expression of the  $\lambda$  Red Gam, Exo, and Beta proteins or recE and recT proteins may be regulated. Thus, the cells may have an increased frequency of homologous recombination as a result of any combination of the aforementioned characteristics. For example, in some embodiments, the cell may carry the sbcA and recBC mutations.

In some embodiments, a linear double stranded DNA to be inserted into the chromosome of the organism is introduced into an organism constitutively or conditionally expressing the recE and recT or the  $\lambda$  Beta, Gam and Exo proteins or proteins with analogous functions as described above. In some embodiments, the organism may be *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*,

*Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* or any species falling within the genera of any of the above species. In some  
 5 embodiments, the double stranded DNA may be introduced into an organism having the recBC and sbcA mutations or analogous mutations.

In other embodiments, a single stranded DNA to be inserted into the chromosome of the organism is introduced into an organism expressing the  $\lambda$  Beta protein or a protein with an analogous function. In some embodiments the single stranded DNA is introduced into an organism  
 10 expressing both the  $\lambda$  Beta and Gam proteins or proteins with analogous functions. In further embodiments, the single stranded DNA is introduced into an organism expressing the  $\lambda$  Beta, Gam and Exo proteins or proteins with analogous functions. The  $\lambda$  proteins or analogous proteins may be expressed constitutively or conditionally. In some embodiments, the organism may be  
 15 *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*,  
 20 *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*,  
 25 *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*,  
 30 *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* or any species falling within the genera of any of the above species.

35 In some embodiments, the linear nucleic acid may be introduced into the chromosome of a first organism which has an enhanced frequency of homologous recombination and then transferred to a second organism which is less amenable to direct application of the present methods. For example, the linear nucleic acid may be introduced into the chromosome of *E. coli* and transferred

into a second organism via conjugation or transduction. After introduction into the second organism, the nucleic acid is inserted into the chromosome of the second organism via homologous recombination, thereby effectively transferring the regulatory element from the chromosome of the first organism into the corresponding location in the chromosome of the second organism.

5 In other embodiments, the cells may be diploid cells, such as fungal cells. In some embodiments, one copy of the gene encoding the proliferation-required gene product may be disrupted, rendering it inactive. In further embodiments, one copy of the gene encoding the proliferation-required gene product may be disrupted and the other copy of the gene encoding the proliferation-required gene product may be placed under the control of a regulatable promoter.

10 Such strains may be generated by disrupting the first copy of the gene encoding the proliferation-required gene product by homologous recombination using a disruption cassette comprising a nucleotide sequence encoding an expressible dominant selectable marker flanked on each side by nucleic acids homologous to the target sequence to be disrupted. The second copy of the gene encoding the proliferation-required gene product may be placed under the control of a regulatable

15 promoter by homologous recombination using a promoter replacement cassette comprising a regulatable promoter flanked on each side by nucleic acids homologous to the natural promoter for the proliferation-required gene. The promoter replacement cassette may also include a nucleotide sequence encoding a selectable marker located 5' of the regulatable promoter but between the nucleic acids homologous to the natural promoter.

20 In other embodiments, overexpression may be achieved by operably linking a proliferation-required gene product described herein to a desired promoter in a vector. The vector may be a vector which replicates extrachromosomally or a vector which integrates into the chromosome. For example, if the vector is to be used in bacterial cells, the vector may be a pBR322 based vector or a bacteriophage based vector such as P1 or lambda. If the vector is to be used in *Saccharomyces*

25 *cerevisiae*, it may be a vector based on the 2 micron circle or a vector incorporating a yeast chromosomal origin of replication. If the vector is to be used in mammalian cells, it may be a retroviral vector, SV40 based vector, a vector based on bovine papilloma virus, a vector based on adenovirus, or a vector based on adeno-associated virus. If the vector is to be used in *Candida albicans* it may be a vector comprising a promoter selected from the group consisting of the

30 CaPCK1, MET25, MAL2, PHO5, GAL1,10, STE2 or STE3 promoters. In some embodiments, the vectors described in the following publications may be used: Clp10, an efficient and convenient integrating vector for *Candida albicans*. Murad et al., Yeast 16(4):325-7 (2000); Transforming vector pCPW7, Kvaal et al., : Infect Immun 67(12):6652-62 (1999); Transforming vector pCWOP16, Kvaal et al., : Infect Immun 65(11):4668-75 (1997); double-ARS vector, pRM1, to be

35 used for direct cloning in Ca by complementation of the histidine auxotrophy of strain CA9, Pla et al., Gene 165(1):115-20 (1995); pMK16, that was developed for the transformation of *C. albicans* and carries an ADE2 gene marker and a *Candida* autonomously replicating sequence (CARS) element promoting autonomous replication (cited in Sanglard and Fiechter Yeast 8(12):1065-75

(1992); A plasmid vector (denoted pRC2312) was constructed, which replicates autonomously in *Escherichia coli*, *Saccharomyces cerevisiae* and *Candida albicans*. It contains LEU2, URA3 and an autonomously replicating sequence (ARS) from *C. albicans*, Cannon et al., Mol Gen Genet 235(2-3):453-7 (1992); Expression vector (Cip10-MAL2p) for use in *Candida albicans* has been  
 5 constructed in which a gene of interest can be placed under the control of the CaMAL2 maltase promoter and stably integrated at the CaRP10 locus (Backen et al., Yeast 16(12):1121-9 (2000)); (Volker, R. S., A. Sonneborn, C. E. Leuker, and J. F. Ernst. 1997. Efg1p, an essential regulator of morphogenesis of the human pathogen *Candida albicans*, is a member of a conserved class of bHLH proteins regulating morphogenetic processes in fungi. EMBO 16:1982-1991.); and a *C.*  
 10 *albicans* transformation vector containing the *C. albicans* URA3 gene, a Candida ARS sequence, and a portion of the *Saccharomyces cerevisiae* 2 microns circle containing the replication origin was constructed. Goshorn et al., Infect Immun 60(3):876-84 (1992). A variety of other vectors suitable for use in foregoing organisms or in any other organism in which the present invention is to be practiced are familiar to those skilled in the art.

15 Underexpression of a proliferation-required gene product described herein may be obtained in a variety of ways. For example, in one embodiment underexpression of the proliferation-required gene product may be achieved by providing an agent, such as an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, an antisense nucleic acid comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400,  
 20 or 500 consecutive nucleotides of a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a nucleic acid complementary to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 6214-42397, a nucleic acid complementary to a nucleic acid comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides of a nucleotide sequence selected from the group consisting of SEQ ID  
 25 NOs.: 6214-42397, a nucleic acid complementary to a nucleic acid which encodes a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42398-78581, a nucleic acid complementary to a nucleic acid which encodes at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids of a polypeptide sequence selected from the group consisting of SEQ ID NOs.: 42398-78581, a homologous antisense nucleic acid, an antisense  
 30 nucleic acid comprising at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides of a homologous nucleic acid, a nucleic acid complementary to a homologous coding nucleic acid, a nucleic acid complementary to at least 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, 150, 200, 300, 400, or 500 consecutive nucleotides of a homologous coding nucleic acid, a nucleic acid complementary to a nucleic acid which encodes a homologous polypeptide, or a  
 35 nucleic acid complementary to a nucleic acid which encodes at least 5, 10, 15, 20, 25, 30, 35, 40, 50, 75, 100, or 150 consecutive amino acids of a homologous polypeptide, which reduces the level or activity of the gene product within the cell. In one embodiment, the agent may comprise an antisense nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ



ID NOs.: 1-6213 which is complementary to a nucleic acid encoding the proliferation-required gene product or complementary to a portion of a nucleic acid encoding the proliferation-required gene product.

5 In one example of antisense-inhibition-based underexpression, a nucleic acid which encodes the antisense nucleic acid may be operably linked to a regulatable promoter. When grown under appropriate conditions, such as media containing an inducer of transcription or an agent which alleviates repression of transcription, the antisense nucleic acid is expressed in the cell, thereby reducing the level or activity of the gene product within the cell. In some embodiments, the concentration of the inducer of transcription or the agent which alleviates repression of transcription  
10 may be varied to provide optimal results. Such methods have been described previously herein and in U.S. Patent Application Serial Number 09/815,242, U.S. Patent Application Serial Number 09/492,709, U.S. Patent Application Serial Number 09/711,164, or U.S. Patent Application Serial Number 09/741,669.

Alternatively, underexpression of a proliferation-required gene product described herein  
15 may be achieved by constructing strains in which the expression of the gene product is under the control of a constitutive or regulatable promoter using methods such as those described above with respect to methods in which the gene product is overexpressed. To provide cells which underexpress the gene product, the cells are grown under conditions in which the gene product is expressed at a level lower than that of a wild type cell. For example, the cells may be grown under  
20 conditions in which a repressor reduces the level of transcription from the regulatable promoter.

In other embodiments, underexpression may be achieved by operably linking the gene required for proliferation to a desired promoter in a vector as described above with respect to  
embodiments in which gene products required for proliferation are overexpressed. In some  
embodiments, the vector may be present in cells in which the chromosomal copy or copies of the  
25 gene has been disrupted.

Examples of gene products, which are encoded by genes that can be underexpressed using methods such as those described above with respect to methods in which the gene product is overexpressed include a gene product whose activity or level is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a  
30 gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 6214-42397, a gene product comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42398-78581, a gene product whose activity or level is inhibited by a homologous antisense nucleic acid, a gene product encoded by a homologous coding nucleic acid, and a gene product comprising a homologous polypeptide.

35 One embodiment of the invention includes a method for identifying a gene product described herein on which a compound which inhibits the proliferation of an organism acts. The method employs a culture which comprises a mixture of strains of the organism. At least some of the strains in the culture overexpress a different gene product which is required for the proliferation

of the organism. Preferably, each of the strains in the culture overexpresses a different gene product which is required for proliferation of the organism (i.e. all of the strains in the culture overexpress a gene product which is required for proliferation of the organism). For example, the gene product which is overexpressed in each strain may be a gene product whose activity or level is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 6214-42397, a gene product comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42398-78581, a gene product whose activity or level is inhibited by a homologous antisense nucleic acid, a gene product encoded by a homologous coding nucleic acid, and a gene product comprising a homologous polypeptide.

Strains that overexpress the proliferation-required gene product may be obtained using the methods described above. The culture may comprise any number of strains which overexpress a gene product required for proliferation. For example the culture may comprise at least two strains, at least 10 strains, at least 20 strains, at least 30, strains, at least 50 strains, at least 100 strains, at least 300 strains or more than 300 strains which overexpress a gene product required for proliferation. In some embodiments, the culture may comprise strains which in aggregate overexpress all or most of the gene products required for proliferation of the organism.

The culture is contacted with a compound which inhibits proliferation of the organism. The compound may be a candidate drug compound obtained from any source. For example, the compound may be a compound generated using combinatorial chemistry, a compound from a natural product library, or an impure or partially purified compound, such as a compound in a partially purified natural extract. The culture is contacted with a sufficient concentration of the compound to inhibit the proliferation of strains of the organism in the culture which do not overexpress the gene product on which the compound acts, such that strains which overexpress said gene product on which the compound acts proliferate more rapidly in the culture than strains which do not overexpress said gene product on which said compound acts. Thus, after a sufficient period of time, the strain which overexpresses the gene product on which the compound acts will be more prevalent in the culture than strains which do not overexpress the gene product on which the compound acts. In a preferred embodiment, the growth conditions and incubation period are selected so that only one strain, the strain overexpressing the target of the compound, is recovered from the culture. Thus, in one embodiment, a plurality of cultures containing a plurality of strains each of which overexpresses a different proliferation-required gene product may be grown in the presence of varying concentrations of the compound. In addition to varying the compound concentrations, in embodiments where expression of the proliferation-required gene product is under the control of a regulatable promoter, the plurality of cultures may be grown at varying concentrations of an agent which regulates the level of expression from the promoter, such as an inducer or an agent which reduces the effect of a repressor on transcription from the promoter. It

will be appreciated, that the cultures may be grown in liquid medium in the presence of the compound whose target is to be identified (and where appropriate in the presence of an agent which regulates the level of expression from the promoter) or alternatively, a liquid culture comprising the strains which overexpress the proliferation-required gene products may be grown in the absence of the compound whose target is to be identified and then introduced onto a solid medium containing the compound (and, where appropriate, also containing an agent which regulates the level of expression from the promoter).

The identity of the overexpressed gene product which is the target of the compound may be determined using a variety of methods. For example, in some embodiments of the present invention, the nucleic acids present in the culture or collection of strains which was contacted with the compound may be compared to the nucleic acids present in a control culture or collection of strains which was not contacted with the compound to identify nucleic acids which are overrepresented in the culture or collection of strains contacted with the test compound relative to the control culture or collection of strains. Alternatively, in some embodiments, the nucleic acids present in a culture or collection of strains contacted with the test compound may be analyzed to identify those nucleic acids which are present without comparison to a control culture or collection of strains.

In some embodiments, the strains which proliferated more rapidly in the culture or collection of strains, i.e. strains having an enhanced ability to proliferate in the presence of a test compound relative to other strains in the culture or collection of strains, are identified as follows. Amplification products which are correlated with each of the overexpressed genes and which are distinguishable from one another are obtained from a culture or collection grown in the presence of a test compound. The amplification products are distinguished from one another to determine whether a particular amplification product is overrepresented in the culture or collection of strains. In some embodiments, the amplification products corresponding to each of the gene products have lengths which permit them to be distinguished from one another. In another embodiment, one or more of the amplification products have similar or identical lengths but are distinguishable from one another based on a detectable agent, such as a dye, attached thereto. In some embodiments, amplification products which are overrepresented are identified by comparing the amplification products from the culture or collection of strains which was contacted with the test compound to the amplification products from a culture or collection of strains which was not contacted with the test compound. Alternatively, amplification products which are overrepresented may be identified by simply identifying the amplification products obtained from the culture or collection of strains contacted with the test compound (for example, only one or a few strains may have proliferated in the presence of the test compound). The above methods for generating distinguishable amplification products may be used in conjunction with any of the methods for generating strains which overexpress gene products required for proliferation described herein in order to facilitate the

identification of strains which proliferate more rapidly or more slowly in the presence of a test compound.

For example, in some embodiments of the present invention, each of the native promoters of each of the genes encoding gene product required for proliferation are replaced by a single  
5 desired replacement promoter. After growth of the culture or collection of strains containing the strains in which the promoters have been replaced in the presence of a test compound for a desired period of time, an amplification reaction is performed on nucleic acids obtained from the culture as follows.

The nucleic acids from the culture or collection of strains may be divided into at least two  
10 aliquots if desired. In a preferred embodiment the nucleic acids from the culture or collection of strains are divided into four aliquots. A single primer complementary to a nucleotide sequence within the replacement promoter, within the proliferation required genes, or within nucleic acid sequences adjacent to the promoter or proliferation required genes is divided into at least two portions, one portion for each aliquot of nucleic acids. Each portion of the primer is labeled with a  
15 distinct detectable dye, such as the 6FAM<sup>TM</sup>, TET<sup>TM</sup>, VIC<sup>TM</sup>, HEX<sup>TM</sup>, NED<sup>TM</sup>, and PET<sup>TM</sup> dyes obtainable from Applied Biosystems (Foster City, CA). For example, the DS-31 or DS-33 dye sets available from Applied Biosystems (Foster City, CA) may be used to label the primers. Alternatively, the HEX<sup>TM</sup>, NED, JOE, TMR and TET<sup>TM</sup> dyes available from Amersham Biosciences may be used. Thus, if the nucleic acids from the culture are not divided into aliquots, a  
20 single primer labeled with a single dye may be used. If the nucleic acids from the culture are divided into aliquots, at least 2, at least 3, at least 4 or more than 4 primers labeled with distinguishable dyes may be used. Each of the portions of labeled primers are added to each of the aliquots of the nucleic acids from the culture or collection of strains such that each aliquot of nucleic acid receives a single labeled primer with a single detectable dye thereon. In some  
25 embodiments, the primers are divided into 3 portions, 4 portions or more than 4 portions, with each portion having a dye which is distinguishable from the dyes on the other portions thereon.

Each of the aliquots of nucleic acids also receives a set of unlabeled primers, with each of the unlabeled primers being complementary to a nucleotide sequence within the promoter, within a nucleotide sequence which is unique to one of the genes encoding gene products required for  
30 proliferation which were placed under the control of the replacement promoter, or within nucleotide sequences adjacent to the promoter or proliferation required genes. Each of the aliquots receives primers unique to 1/N proliferation required genes which were placed under the control of the replacement promoter, where N is the number of aliquots (i.e. if the culture or collection of strains consisted of 100 strains in which a gene required for proliferation was placed under the control of  
35 the replacement promoter and was divided into four aliquots, then each of the four aliquots of nucleic acids from the culture or collection of strains would receive primers complementary to 25 of the genes). The unlabeled primers are selected so that each will yield an amplification product having a length distinguishable from the length of the amplification product produced with the other

unlabeled primers. Preferably, the amplification products are between about 100-about 400 nucleotides in length, but any lengths which may be distinguished from each other may be used. In addition, in some of the embodiments some of the amplification products may have identical or very similar lengths but be distinguishable from one another due to labeling with distinguishable dyes.

A nucleic acid amplification reaction is conducted on each of the nucleic acid aliquots. The amplification products are then separated by length to identify amplification products having increased representation in the culture or collection of strains (i.e. amplification products derived from cells which proliferated more rapidly in the culture or collection of strains). The amplification products are then correlated with the corresponding genes to determine which strains proliferated more rapidly in the culture or collection of strains. If desired, amplification products having increased representation in the culture may be identified by comparing the amplification products obtained from a culture or collection of strains which was contacted with the compound to amplification products obtained from a control culture or collection of strains which was not contacted with the compound. Alternatively, if desired, the amplification products which are obtained from a culture which was contacted with the compound may be directly identified without comparison to a control culture which was not contacted with the compound.

For example, in some embodiments, the amplification products from each of the nucleic acid aliquots are pooled and subjected to capillary electrophoresis. The amplification products are detected by detecting the fluorescent dyes attached thereto and their lengths are determined to identify those amplification products having increased or decreased representation in the culture or collection of strains. Figures 2A and 2B illustrate one embodiment of this method in which the absence of an amplification product from an amplification reaction performed on a culture comprising a plurality of strains underexpressing genes required for proliferation indicates that a test compound acts on the gene corresponding to the missing amplification product. It will be appreciated that the method may also be used to identify an amplification product which is overrepresented in an amplification reaction conducted on a culture or collection of strains overexpressing genes required for proliferation because the test compound acted on the corresponding gene.

Alternatively, in another embodiment, a first amplification reaction is performed on nucleic acids obtained from a culture or collection of strains which was contacted with the compound using a first primer complementary to a nucleotide sequence present upstream or downstream of all of the overexpressed genes (such as a primer complementary to a nucleotide sequence in a replacement promoter upstream of all of the overexpressed genes) and a set of primers complementary to a nucleotide sequence unique to each of the strains (such as a primer complementary to a nucleotide sequence within each of the proliferation-required genes). One of the two amplification primers for each of the proliferation required genes is labeled with a dye as described above. Preferably, the common primer complementary to a nucleotide sequence upstream or downstream of all of the

overexpressed genes is labeled with the dye. The primers used in the amplification reaction are designed so that the amplification product corresponding to each proliferation-required gene has a unique length or a dye which allows it to be distinguished from other amplification products of the same length. A second amplification reaction is conducted on a control culture or collection of strains which was not contacted with the compound using the same primers as in the first amplification reaction. The amplification products from the first amplification reaction are compared to those from the second amplification reaction to identify one or more amplification products which are overrepresented in the culture or collection of strains. For example, the amplification products from the first amplification reaction may be run in a separate lane of a polyacrylamide gel or a separate capillary than the amplification products from the second amplification reaction and the two lanes or capillaries are compared to one another. If desired, in the embodiment where the amplification products from the first amplification reaction are run in a different lane or capillary than the amplification products from the second amplification reaction, the same dye may be used to label the primers in the first and second amplification reactions. Alternatively, if desired, different dyes may be used to label the primers in the first and second amplification reactions. If desired, in the embodiment where the amplification products from the first amplification reaction are run in a different lane or capillary than the amplification products from the second amplification reaction, the same dye may be used to label the primers in the first and second amplification reactions. Alternatively, if desired, different dyes may be used to label the primers in the first and second amplification reactions.

Alternatively, in some embodiments, the primers in the second amplification reaction are labeled with a different dye which is distinguishable from the dye used in the first amplification reaction. In this embodiment, the amplification reactions may be pooled and run in the same lane on a polyacrylamide gel or in the same capillary and the products from each amplification reaction are compared by comparing the amount of each dye present for each amplification product. Figures 3A and 3B illustrate one embodiment of this method in which the absence of an amplification product from the amplification reaction performed on a culture comprising a plurality of strains underexpressing genes required for proliferation which was contacted with the compound indicates that a test compound acts on the gene corresponding to the missing amplification product. It will be appreciated that the method may also be used to identify an amplification product which is overrepresented in an amplification reaction conducted on a culture or collection of strains overexpressing genes required for proliferation because the test compound acted on the corresponding gene.

If desired, rather than dividing the culture into aliquots, individual amplification reactions may be conducted on nucleic acids obtained from the culture or collection of strains. Each amplification reaction contains primers which will yield an amplification product specific for only one of the proliferation required genes. The resulting amplification products from each of the

individual amplification reactions are pooled and amplification products having increased representation in the culture are identified as described above.

In another embodiment, a culture or collection of strains in which gene products required for proliferation are overexpressed from regulatable promoters which replaced the native promoters of the genes encoding these gene products is allowed to grow in the presence of a test compound for a desired number of generations. Preferably, the culture or collection of strains is allowed to grow in the presence of the test compound for at least 20 generations. Nucleic acids are isolated from the culture or collection of strains and an amplification reaction is performed using a primer which is complementary to a nucleotide sequence within the replacement promoter(s) or a nucleotide sequence adjacent to the 5' end thereof and primers which are complementary to a nucleotide sequence within the proliferation required genes or nucleotide sequences adjacent thereto. The resulting amplification product(s) is directly sequenced using a primer complementary to a nucleotide sequence within the replacement promoter.

In one embodiment of the present invention, the vector containing the nucleotide sequence encoding the proliferation-required gene product is obtained from a strain which proliferated more rapidly in the culture using methods such as plasmid preparation techniques. Nucleic acid sequencing techniques are then employed to determine the nucleotide sequence of the gene which was overexpressed.

Alternatively, the identity of the overexpressed gene product which is the target of the compound may be determined by performing a nucleic acid amplification reaction, such as a polymerase chain reaction (PCR), to identify the nucleotide sequence of the gene which was overexpressed. For example, aliquots of a nucleic acid preparation, such as a purified plasmid, from the strain which is recovered from the culture may each be contacted with pairs of PCR primers which would amplify a different proliferation-required gene to determine which pair of primers yields an amplification product.

An alternative method for determining the identity of the gene product described herein which is the target of the compound involves obtaining a nucleic acid array, such as a DNA chip, which contains each of the proliferation-required genes which were overexpressed in the strains in the culture. Each proliferation-required gene occupies a known location in the array. A nucleic acid preparation, such as a plasmid preparation, from the recovered strain is labeled with a detectable agent, such as radioactive or fluorescent moiety, and placed in contact with the nucleic acid array under conditions which permit the labeled nucleic acid to hybridize to complementary nucleic acids on the array. The location on the array to which the labeled nucleic acids hybridize is determined to identify the gene which was overexpressed in the recovered strain. If desired the hybridized nucleic acids from a culture which was contacted with the compound may be compared to the hybridized nucleic acids from a control culture which was not contacted with the compound. Alternatively, the hybridized nucleic acids from a culture which was contacted with the compound may be directly identified without comparison to nucleic acids from a control culture.

In some instances, more than one strain may proliferate more rapidly in the presence of the compound. This may result from a variety of causes. For example, the concentration of the compound may not have been high enough to restrict proliferation only to cells which overexpress one gene product (i.e. the target gene product). While strains which overexpress the target gene product will be the most prevalent strain in the culture, other strains may also have proliferated. In such instances, the identity of the gene product in the strain which is most prevalent in the culture may be identified by quantitating the levels of each of the genes encoding proliferation-required proteins in the culture. This may be accomplished by quantitative PCR, DNA sequencing, hybridization, or array technology as described above.

In other instances, multiple strains will exhibit more rapid proliferation in the culture as a result of a common functional attribute. For example, the strains which proliferate more rapidly may each overexpress a gene product with a common enzymatic activity, such as serine protease activity for example. Alternatively, the strains which proliferate more rapidly may each overexpress a gene product with a common functional domain, such as a cAMP binding domain. In such instances, the common attribute of the strains which proliferate more rapidly may provide information as to the mode of action of the compound or the biochemical activity of the target of the compound. For example, if all of the overexpressed genes in the strains which proliferated more rapidly are serine proteases, the compound acts by inhibiting serine protease activity and the target protein is a serine protease. If desired, the compound may be derivatized and the efficacy of the derivatized compound against each of the strains which proliferated more rapidly may be assessed as described herein in order to identify derivatives which are capable of interacting with a wide range of targets sharing a common activity or binding site (i.e. derivatives which have a greater ability to inhibit the proliferation of all the strains than the original compound) or to identify derivatives having greater specificity for a desired target (i.e. derivatives which have a greater specificity for one of the strains than the original compound). For example, it is possible that a nonessential gene product expressed in the cell might also bind to the initial test compound in addition to the gene product required for proliferation. In such an instance, it is desirable to obtain a derivative of the initial test compound which is specific for the gene product required for proliferation. In addition, it is possible that two gene products required for proliferation might bind to the initial test compound but specificity for one of the gene products is desired.

Rather than employing a single culture which contains multiple strains each of which overexpresses a proliferation-required gene product described herein, the methods of the present invention may be performed using an array of individual strains (i.e. a collection of strains) each of which overexpresses a different proliferation-required gene product. For example, individual strains each overexpressing a different proliferation-required gene product may be grown in different wells of a multiwell plate. Each well is contacted with the compound (and, where appropriate an agent which regulates the level of expression from the promoter). The level of proliferation of the strains in each of the wells is determined to identify a strain which proliferated



more rapidly. The identity of the overexpressed gene product in the strain that proliferated more rapidly is determined as described above.

In another embodiment, individual strains each overexpressing a different proliferation-required gene product (i.e. a collection of strains) are grown at different locations on a solid medium, such as an agar plate. The medium contains the compound and where appropriate an agent which regulates the level of expression from the promoter). The level of proliferation of each of the strains is determined to identify a strain which proliferated more rapidly. The identity of the overexpressed gene product in the strain that proliferated more rapidly is determined as described above.

The above methods may be used to prioritize compound development or to determine whether the compound has been previously identified or whether the target of the compound is the target of a previously identified drug. In particular, if the product is a natural product, it is advantageous to determine whether it has been previously identified prior to investing significant effort in developing it. Thus, in some embodiments of the present invention, the target of a partially purified or purified natural product or a compound produced by combinatorial chemistry is identified using the methods described above and compared to the targets of known drugs. If the target is identical to that of a known drug, further development of the compound is halted.

Alternatively, an array of strains each of which overexpresses a different gene product described herein (i.e. a collection of strains) is grown on solid medium containing a compound to be evaluated. The location of each strain in the array and the gene product overexpressed by that strain is known. The pattern of colonies which grow in the presence of the compound is evaluated and compared to the pattern of colonies which grow in the presence of previously identified drugs. If the pattern of colonies which grow in the presence of the compound being evaluated is the same as the pattern of colonies which grow in the presence of a previously identified drug, further development of the compound is halted.

Additionally in some embodiments, the sequence of the gene product in a strain which proliferated more rapidly in the assays described above is compared to the sequence of gene products from heterologous organisms to determine the likely spectrum of species whose growth would be inhibited by the compound. If the gene product has a high degree of homology to gene products from heterologous species, it is likely that the compound would also inhibit the growth of these heterologous species. Homology may be determined using any of a variety of methods familiar to those skilled in the art. For example, homology may be determined using a computer program such as BLASTP or FASTA. The ability of the compound to inhibit the growth of the heterologous species may then be confirmed by comparing the growth of cells of the heterologous species in the presence and absence of the compound.

Current methods for identifying the target of compounds which inhibit cellular proliferation are laborious and time consuming. The above methods may be employed to allow the targets of a large number of compounds to be rapidly identified. In such methods, the methods described above

are simultaneously performed for each of a large number of compounds. For example, the compounds may be members of a library of compounds generated using combinatorial chemistry or members of a natural product library. In such methods, a plurality of cultures each comprising a plurality of strains each of which overexpresses a different gene product required for proliferation  
5 or a plurality of collections of individual strains each of which overexpresses a different gene product required for proliferation is obtained. Each culture or collection of strains is contacted with a different compound in the library and the target of the compound is identified as described above.

In another embodiment, the gene product described herein on which a compound which inhibits the proliferation of an organism acts is identified using a culture which comprises a mixture  
10 of strains of the organism including strains which underexpress a different gene product which is required for proliferation of the organism (i.e. at least some of the strains in the culture underexpress a gene product which is required for proliferation of the organism). Preferably, each of the strains in the culture underexpress a different a gene product which is required for the proliferation of the organism (i.e. all of the strains in the culture underexpress a gene product which  
15 is required for the proliferation of the organism). In some embodiments, the culture comprises at least one strain which underexpresses a gene product selected from the group consisting of a gene product whose activity or level is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 6214-  
20 42397, a gene product comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42398-78581, a gene product whose activity or level is inhibited by a homologous antisense nucleic acid, a gene product encoded by a homologous coding nucleic acid, and a gene product comprising a homologous polypeptide.

Strains underexpressing the proliferation-required gene products described herein may be  
25 obtained using the methods described above. The culture may comprise any number of strains. For example the culture may comprise at least two strains, at least 10 strains, at least 20 strains, at least 30, strains, at least 50 strains, at least 100 strains, at least 300 strains or more than 300 strains which underexpress a gene product required for proliferation. In some embodiments, the strains in the culture in aggregate may underexpress all or most of the gene products required for proliferation of  
30 the organism.

The culture is contacted with a compound which inhibits proliferation of the organism. The compound may be a candidate drug compound obtained from any source. For example, the compound may be a compound generated using combinatorial chemistry, a compound from a natural product library, or an impure or partially purified compound, such as a compound in a  
35 partially purified natural extract. The culture is contacted with a sufficient concentration of the compound to inhibit the proliferation of strains of the organism in the culture which underexpress the gene product on which the compound acts, such that strains which do not underexpress the gene product on which the compound acts proliferate more rapidly in the culture than strains which do

underexpress said gene product on which said compound acts. Thus, after a sufficient period of time, the strain which underexpresses the gene product on which the compound acts will be less prevalent in the culture than strains which do not underexpress the gene product on which the compound acts. In one embodiment, the growth conditions and incubation period are selected so that only one strain, the strain underexpressing the target of the compound, proliferates at a reduced rate in the culture. In another embodiment, the growth conditions may be selected so that the strain underexpressing the target of the compound is not recovered from the culture. Thus, in one embodiment, a plurality of cultures containing a plurality of strains each of which underexpresses a different proliferation-required gene product may be grown in the presence of varying concentrations of the compound. In addition to varying the compound concentrations, in embodiments where expression of the proliferation-required gene product is under the control of a regulatable promoter, the plurality of cultures may be grown at varying concentrations of an agent which regulates the level of expression from the promoter, such as an inducer or an agent which reduces the effect of a repressor on transcription from the promoter. It will be appreciated, that the cultures may be grown in liquid medium in the presence of the compound whose target is to be identified (and where appropriate in the presence of an agent which regulates the level of expression from the promoter) or alternatively, a liquid culture comprising the strains which underexpress the proliferation-required gene products may be grown in the absence of the compound whose target is to be identified and then introduced onto a solid medium containing the compound (and, where appropriate, also containing an agent which regulates the level of expression from the promoter).

The identity of the underexpressed gene product which is the target of the compound may be determined using a variety of methods. For example, in some embodiments of the present invention, the nucleic acids present in the culture or collection of strains which was contacted with the compound may be compared to the nucleic acids present in a control culture or collection of strains which was not contacted with the compound to identify nucleic acids which are underrepresented in the culture or collection of strains contacted with the test compound relative to the control culture or strains. Alternatively, in some embodiments, the nucleic acids present in a culture or collection of strains contacted with the test compound may be analyzed to identify those nucleic acids which are missing or present at reduced levels without comparison to a control culture or collection of strains.

In some embodiments of the present invention, the strains which proliferated more slowly in the culture or collection of strains, i.e. strains having an decreased ability to proliferate in the presence of a test compound or which do not proliferate in the presence of a test compound, are identified as follows. Amplification products which are correlated with each of the underexpressed genes and which are distinguishable from one another are obtained from a culture or collection grown in the presence of a test compound. The amplification products are distinguished from one another to determine whether a particular amplification product is underrepresented in the culture or collection of strains. In some embodiments, the amplification products corresponding to each of the

gene products have lengths which permit them to be distinguished from one another. In another embodiment, one or more of the amplification products have similar or identical lengths but are distinguishable from one another based on a detectable agent, such as a dye, attached thereto. In some embodiments, amplification products which are underrepresented are identified by comparing the amplification products from the culture or collection of strains which was contacted with the test compound to the amplification products from a culture or collection of strains which was not contacted with the test compound. Alternatively, amplification products which are underrepresented in the culture or collection of strains may be identified simply by determining which amplification products are missing or present at reduced levels in the culture or collection of strains. The above methods for generating distinguishable amplification products may be used in conjunction with any of the methods for generating strains which underexpress gene products required for proliferation described herein in order to facilitate the identification of strains which proliferate more slowly in the presence of a test compound.

For example, in some embodiments of the present invention, each of the native promoters of each of the genes encoding gene product required for proliferation are replaced by a single desired replacement promoter. After growth of the culture or collection of strains containing the strains in which the promoters have been replaced in the presence of a test compound for a desired period of time, an amplification reaction is performed on nucleic acids obtained from the culture as follows.

The nucleic acids from the culture or collection of strains are divided into at least two aliquots. In a preferred embodiment the nucleic acids from the culture or collection of strains are divided into four aliquots. A single primer complementary to a nucleotide sequence within the replacement promoter, within the proliferation required genes, or within nucleic acid sequences adjacent to the promoter or proliferation required genes is divided into four groups. Each group is labeled with a distinct detectable dye, such as the 6FAM<sup>TM</sup>, TET<sup>TM</sup>, VIC<sup>TM</sup>, HEX<sup>TM</sup>, NED<sup>TM</sup>, and PET<sup>TM</sup> dyes obtainable from Applied Biosystems (Foster City, CA). For example, the DS-31 or DS-33 dye sets available from Applied Biosystems (Foster City, CA) may be used to label the primers. Each of the groups of labeled primers are added to each of the aliquots of the nucleic acids from the culture or collection of strains such that each aliquot of nucleic acid receives a single labeled primer with a single detectable dye thereon.

Each of the aliquots of nucleic acids also receives a set of unlabeled primers, with each of the unlabeled primers being complementary to a nucleotide sequence within the promoter, within a nucleotide sequence which is unique to one of the genes encoding gene products required for proliferation which were placed under the control of the replacement promoter, or within nucleotide sequences adjacent to the promoter or proliferation required genes. Each of the aliquots receives primers unique to 1/N proliferation required genes which were placed under the control of the replacement promoter, where N is the number of aliquots (i.e. if the culture or collection of strains consisted of 100 strains in which a gene required for proliferation was placed under the control of the replacement promoter and was divided into four aliquots, then each of the four aliquots of

nucleic acids from the culture or collection of strains would receive primers complementary to 25 of the genes). The unlabeled primers are selected so that each will yield an amplification product having a length distinguishable from the length of the amplification product produced with the other unlabeled primers. Preferably, the amplification products are between about 100-about 400  
5 nucleotides in length, but any lengths which may be distinguished from each other may be used. In addition, in some of the embodiments some of the amplification products may have identical or very similar lengths but be distinguishable from one another due to labeling with distinguishable dyes.

A nucleic acid amplification reaction is conducted on each of the nucleic acid aliquots. The  
10 amplification products are then separated by length to identify amplification products decreased representation or which are absent in the culture or collection of strains. The amplification products are then correlated with the corresponding genes to determine which strains proliferated more slowly in the culture or collection of strains. If desired, amplification products having decreased representation in the culture may be identified by comparing the amplification products obtained  
15 from a culture or collection of strains which was contacted with the compound to amplification products obtained from a control culture or collection of strains which was not contacted with the compound. Alternatively, if desired, the amplification products which are missing or present at reduced levels in a culture which was contacted with the compound may be directly identified without comparison to a control culture which was not contacted with the compound.

For example, in some embodiments, the amplification products from each of the nucleic  
20 acid aliquots are pooled and subjected to capillary electrophoresis. The amplification products are detected by detecting the fluorescent dyes attached thereto and their lengths are determined to identify those amplification products having decreased representation in the culture or collection of strains. Figures 2A and 2B illustrate one embodiment of this method in which the absence of an  
25 amplification product from an amplification reaction performed on a culture comprising a plurality of strains underexpressing genes required for proliferation indicates that a test compound acts on the gene corresponding to the missing amplification product.

Alternatively, in another embodiment, a first amplification reaction is performed on nucleic  
acids obtained from a culture or collection of strains which was contacted with the compound using  
30 a first primer complementary to a nucleotide sequence present upstream or downstream of all of the overexpressed genes (such as a primer complementary to a nucleotide sequence in a replacement promoter upstream of all of the overexpressed genes) and a set of primers complementary to a nucleotide sequence unique to each of the strains (such as a primer complementary to a nucleotide sequence within each of the proliferation-required genes). One of the two amplification primers for  
35 each of the proliferation required genes is labeled with a dye as described above. Preferably, the common primer complementary to a nucleotide sequence upstream or downstream of all of the overexpressed genes is labeled with the dye. The primers used in the amplification reaction are designed so that the amplification product corresponding to each proliferation-required gene has a

unique length. A second amplification reaction is conducted on a control culture or collection of strains which was not contacted with the compound using the same primers as in the first amplification reaction. The amplification products from the first amplification reaction are compared to those from the second amplification reaction to identify one or more amplification products which are underrepresented in the culture or collection of strains. For example, the amplification products from the first amplification reaction may be run in a separate lane of a polyacrylamide gel or a separate capillary than the amplification products from the second amplification reaction and the two lanes or capillaries are compared to one another.

Alternatively, in some embodiments, the primers in the second amplification reaction are labeled with a different dye which is distinguishable from the dye used in the first amplification reaction. In this embodiment, the amplification reactions may be pooled and run in the same lane on a polyacrylamide gel or in the same capillary and the products from each amplification reaction are compared by comparing the amount of each dye present for each amplification product. Figures 3A and 3B illustrate one embodiment of this method in which the absence of an amplification product from the amplification reaction performed on a culture comprising a plurality of strains underexpressing genes required for proliferation which was contacted with the compound indicates that a test compound acts on the gene corresponding to the missing amplification product.

If desired, rather than dividing the culture into aliquots, individual amplification reactions may be conducted on nucleic acids obtained from the culture or collection of strains. Each amplification reaction contains primers which will yield an amplification product specific for only one of the proliferation required genes. The resulting amplification products from each of the individual amplification reactions are pooled and amplification products having decreased representation in the culture are identified as described above.

In an alternative embodiment, the representation of each strain in the culture may be assessed by hybridizing detectably labeled nucleic acids encoding the proliferation-required gene products, or portions thereof, obtained from the culture to an array comprising nucleic acids encoding the gene products required for proliferation or portions thereof. Each nucleic acid encoding a gene product required for proliferation or portion thereof occupies a known location on the array. The signal from each location on the array is quantitated to identify those nucleic acids encoding a proliferation-required gene product which are underrepresented in the culture. If desired the hybridized nucleic acids from a culture which was contacted with the compound may be compared to the hybridized nucleic acids from a control culture which was not contacted with the compound. Alternatively, the hybridized nucleic acids from a culture which was contacted with the compound may be directly analyzed without comparison to nucleic acids from a control culture.

In another alternative, each strain underexpressing a gene product required for proliferation may be constructed to contain a unique nucleic acid sequence (referred to herein as a "tag"). The tag may be included in the chromosome of each strain or in an extrachromosomal vector. For example, the tag could be included in a vector encoding an antisense nucleic acid complementary to

a gene encoding a gene product required for proliferation or a portion of such a gene or the tag may be included in the antisense nucleic acid itself. The representation of each strain in the culture may be assessed by performing an amplification reaction using primers complementary to each of the tags and quantitating the levels of the resulting amplification products to identify a tag which is underrepresented or absent from the culture. Since each tag corresponds to one strain, the strain which is underrepresented or absent from the culture may be identified. If desired the tags present in a culture which was contacted with the compound may be compared to the tags present in a control culture which was not contacted with the compound. Alternatively, the tags present in a culture which was contacted with the compound may be analyzed without comparison to a control culture.

It will be appreciated that, if desired, unique tags may also be used in embodiments in which gene products required for proliferation are overexpressed. In some aspects of such embodiments, the tags may be within or adjacent to the promoter which drives expression of the gene encoding the gene product. In such embodiments, the gene product which is overexpressed in strains which proliferate more rapidly in the culture may be identified by detecting the presence or amount of the unique tag corresponding to that gene product in the culture.

In some instances, more than one strain may proliferate less rapidly in the presence of the compound. This may result from a variety of causes. For example, the concentration of the compound may not have been high enough to reduce the proliferation only in cells which underexpress one gene product (i.e. the target gene product). While strains which underexpress the target gene product will be the least prevalent strain in the culture, other strains may also be underrepresented. In such instances, the identity of the gene product in the strain which is least prevalent in the culture (or not recovered from the culture) may be identified by quantitating the levels of each of the genes encoding proliferation-required proteins in the culture. This may be accomplished by quantitative PCR, DNA sequencing, hybridization, or array technology as described above.

In other instances, multiple strains will exhibit less rapid proliferation in the culture as a result of a common functional attribute. For example, the strains which proliferate less rapidly (or the strains which are not recovered from the culture) may each underexpress a gene product with a common enzymatic activity, such as serine protease activity for example. Alternatively, the strains which proliferate less rapidly (or the strains which are not recovered from the culture) may each underexpress a gene product with a common functional domain, such as a cAMP binding domain. In such instances, the common attribute of the strains which proliferate less rapidly (or the strains which are not recovered from the culture) may provide information as to the mode of action of the compound or the biochemical activity of the target of the compound. For example, if all of the underexpressed genes in the strains which proliferated less rapidly are serine proteases, the compound acts by inhibiting serine protease activity and the target protein is a serine protease. If desired, the compound may be derivatized and the efficacy of the derivatized compound against

each of the strains which proliferated more rapidly may be assessed as described herein in order to identify derivatives which are capable of interacting with a wide range of targets sharing a common activity or binding site (i.e. derivatives which have a greater ability to inhibit the proliferation of all the strains than the original compound) or to identify derivatives having greater specificity for a desired target (i.e. derivatives which have a greater specificity for one of the strains than the original compound).

Rather than employing a single culture which contains multiple strains each of which underexpresses a proliferation-required gene product described herein, the methods of the present invention may be performed using an array of individual strains (i.e. a collection of strains) each of which underexpresses a different proliferation-required gene product. For example, individual strains each underexpressing a different proliferation-required gene product may be grown in different wells of a multiwell plate. Each well is contacted with the compound (and, where appropriate an agent which regulates the level of expression from the promoter). The level of proliferation of the strains in each of the wells is determined to identify a strain which proliferated less rapidly or which did not proliferate at all. The identity of the underexpressed gene product in the strain that proliferated less rapidly or which did not proliferate at all is determined as described above.

In another embodiment, individual strains each underexpressing a different proliferation-required gene product (i.e. a collection of strains) are grown at different locations on a solid medium, such as an agar plate. The medium contains the compound and, where appropriate, an agent which regulates the level of expression from the promoter. The level of proliferation of each of the strains is determined to identify a strain which proliferated less rapidly (or a strain which is not recovered from the culture). The identity of the underexpressed gene product in the strain that proliferated less rapidly (or the strain which is not recovered from the culture) is determined as described above.

The above methods may be used to prioritize compound development or to determine whether the compound has been previously identified or whether the target of the compound is the target of a previously identified drug. In particular, if the product is a natural product is advantageous to determine whether it has been previously identified prior to investing significant effort in developing it. Thus, in some embodiments of the present invention, the target of a partially purified or purified natural product or a compound produced by combinatorial chemistry is identified using the methods described above and compared to the targets of known drugs. If the target is identical to that of a known drug, further development of the compound is halted.

Alternatively, an array of strains each of which underexpresses a different gene product described herein (i.e. a collection of strains) is grown on solid medium containing a compound to be evaluated. The location of each strain in the array and the gene product underexpressed by that strain is known. The pattern of colonies which grow less rapidly or fail to grow in the presence of the compound is evaluated and compared to the pattern of colonies which grow less rapidly or fail



to grow in the presence of previously identified drugs. If the pattern of colonies which grow less rapidly or fail to grow in the presence of the compound being evaluated is the same as the pattern of colonies which grow less rapidly or fail to grow in the presence of a previously identified drug, further development of the compound is halted.

5           Additionally, the nucleotide sequence of the gene product described herein in a strain which proliferated less rapidly (or a strain which was not recovered from the culture) in the assays described above is compared to the nucleotide sequence of gene products from heterologous organisms to determine the likely spectrum of species whose growth would be inhibited by the compound. If the gene product has a high degree of homology to gene products from heterologous  
10 species, it is likely that the compound would also inhibit the growth of these heterologous species. Homology may be determined using any of a variety of methods familiar to those skilled in the art. For example, homology may be determined using a computer program such as BLASTP or FASTA. The ability of the compound to inhibit the growth of the heterologous species may then be confirmed by comparing the growth of cells of the heterologous species in the presence and absence  
15 of the compound.

          In other embodiments, the present invention uses collections or cultures of strains comprising both strains which overexpress gene products described herein required for cellular proliferation and strains which underexpress the same gene products required for cellular proliferation. The gene product which is overexpressed or underexpressed in each strain may be a  
20 gene product whose activity or level is inhibited by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 1-6213, a gene product encoded by a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NOs.: 6214-42397, a gene product comprising an amino acid sequence selected from the group consisting of SEQ ID NOs.: 42398-78581, a gene product whose activity or level is inhibited by a homologous  
25 antisense nucleic acid, a gene product encoded by a homologous coding nucleic acid, and a gene product comprising a homologous polypeptide.

          The culture or collection of strains is contacted with a compound and the nucleic acids present in the culture or collection of strains are analyzed. Preferably, nucleic acids derived from overexpressing strains can be distinguished from those derived from underexpressing strains. For  
30 example, the overexpressing strains may be obtained using promoter replacement as described above while the underexpressing strains may be obtained by expressing antisense nucleic acids. Accordingly, in one embodiment, amplification primers may be designed which will uniquely amplify nucleic acids from the overexpressing strains or the underexpressing strains. If a compound acts on a gene product which was overexpressed and underexpressed in the culture, then  
35 the amplification product obtained from the strain in the culture or collection which overexpressed gene product will be overrepresented in the culture or collection while the amplification product obtained from the strain which underexpressed the gene product will be underrepresented in the culture or collection. If desired, nucleic acids from a culture or collection which was contacted with

the compound may be compared to nucleic acids from a control culture or collection which was not contacted with the compound. Alternatively, nucleic acids from a culture or collection which was contacted with the compound may be directly analyzed without comparison to a control culture or collection.

5           In some embodiments, strains are constructed in which a nucleic acid complementary to a gene encoding a gene product described herein required for proliferation or a portion thereof is operably linked to a regulatable promoter. For example, in some embodiments, the strains may transcribe an antisense nucleic acid selected from the group consisting of SEQ ID NOs.: 1-6213 or fragments thereof which inhibit proliferation or reduce the activity or level of the gene product  
10           encoded by the gene comprising a nucleotide sequence complementary to the antisense nucleic acid or homologous antisense nucleic acids or fragments thereof. In other embodiments, the strains may transcribe an antisense nucleic acid which reduces the activity or level of a gene product encoded by SEQ ID NOs.: 6214-42397, the polypeptides of SEQ ID NOs.: 42398-78581, homologous coding nucleic acids or homologous polypeptides. A culture comprising a plurality of such strains  
15           wherein each strain expresses an antisense nucleic acid against a different gene product required for proliferation is grown in the presence of varying levels of a compound which inhibits proliferation and in the presence of varying levels of an agent which regulates the level of transcription from the regulatable promoter. Nucleic acids samples are obtained from the culture, detectably labeled and hybridized to a solid support comprising nucleic acids containing the genes encoding the  
20           proliferation-required gene products or a portion thereof. The level of hybridization is quantitated for each nucleic acid encoding each of the proliferation-required gene products to determine the rate at which each of the strains proliferated in the culture. If the antisense nucleic acid expressed by a strain in the culture is not complementary to all or a portion of the gene encoding the target of the compound (i.e. a nonspecific strain), then the hybridization intensity for that strain will not be  
25           correlated with the concentration of the compound (See Figure 4), while if the antisense nucleic acid expressed by a strain in the culture is complementary to all or a portion of the gene encoding the target of the compound, the hybridization intensity for that strain will be intimately correlated with the concentration of the compound (See Figure 5). In this manner, the target of the compound may be identified. It will be appreciated that, as described above, rather than growing the strains in  
30           a single culture, each strain may be grown in a different location on a solid medium or in a different well of a multiwell plate.

          The methods described above can be simultaneously performed for each of a large number of compounds. For example, the compounds may be members of a library of compounds generated using combinatorial chemistry or members of a natural product library. In such methods, a plurality  
35           of cultures each comprising a plurality of strains each of which overexpresses or underexpresses a different gene product required for proliferation or a plurality of collections of individual strains each of which overexpresses or underexpresses a different gene product required for proliferation is

obtained. Each culture or collection of strains is contacted with a different compound in the library and the target of the compound is identified as described above.

In still another embodiment, the antisense nucleic acids of the present invention (including the antisense nucleic acids of SEQ ID NOs. 1-6213 fragments thereof or homologous antisense nucleic acids or fragments thereof) that inhibit bacterial growth or proliferation can be used as antisense therapeutics for killing bacteria. The antisense sequences can be complementary to one of SEQ ID NOs.: 6214-42397 or fragments thereof, homologous coding nucleic acids or fragments thereof. Alternatively, antisense therapeutics can be complementary to operons in which proliferation-required genes reside (i.e. the antisense nucleic acid may hybridize to a nucleotide sequence of any gene in the operon in which the proliferation-required genes reside). Further, antisense therapeutics can be complementary to a proliferation-required gene or portion thereof with or without adjacent noncoding sequences, an intragenic sequence (i.e. a sequence within a gene), an intergenic sequence (i.e. a sequence between genes), a sequence spanning at least a portion of two or more genes, a 5' noncoding region or a 3' noncoding region located upstream or downstream from the actual sequence that is required for bacterial proliferation or an operon containing a proliferation-required gene.

In addition to therapeutic applications, the present invention encompasses the use of nucleic acids complementary to nucleic acids required for proliferation as diagnostic tools. For example, nucleic acid probes comprising nucleotide sequences complementary to proliferation-required sequences that are specific for particular species of cells or microorganisms can be used as probes to identify particular microorganism species or cells in clinical specimens. This utility provides a rapid and dependable method by which to identify the causative agent or agents of a bacterial infection. This utility would provide clinicians the ability to accurately identify the species responsible for the infection and administer a compound effective against it. In an extension of this utility, antibodies generated against proteins translated from mRNA transcribed from proliferation-required sequences can also be used to screen for specific cells or microorganisms that produce such proteins in a species-specific manner.

Other embodiments of the present invention include methods of identifying compounds which inhibit the activity of gene products required for cellular proliferation using rational drug design. As discussed in more detail below, in such methods, the structure of the gene product is determined using techniques such as x-ray crystallography or computer modeling. Compounds are screened to identify those which have a structure which would allow them to interact with the gene product or a portion thereof to inhibit its activity. The compounds may be obtained using any of a variety of methods familiar to those skilled in the art, including combinatorial chemistry. In some embodiments, the compounds may be obtained from a natural product library. In some embodiments, compounds having a structure which allows them to interact with the active site of a gene product, such as the active site of an enzyme, or with a portion of the gene product which interacts with another biomolecule to form a complex are identified. If desired, lead compounds may be identified and further optimized to provide compounds which are highly effective against the gene product.

The following examples teach the genes of the present invention and a subset of uses for the genes identified as required for proliferation. These examples are illustrative only and are not intended to limit the scope of the present invention.

### EXAMPLES

5           The following examples are directed to the identification and exploitation of genes required for proliferation. Methods of gene identification are discussed as well as a variety of methods to utilize the identified sequences. It will be appreciated that any of the antisense nucleic acids, proliferation-  
10           required genes or proliferation-required gene products described herein, or portions thereof, may be used in the procedures described below, including the antisense nucleic acids of SEQ ID NOS.: 1-6213, the nucleic acids of SEQ ID NOS.: 6214-42397, or the polypeptides of SEQ ID NOS.: 42398-78581. Likewise, homologous antisense nucleic acids, homologous coding nucleic acids, homologous polypeptides or portions of any of the above-mentioned nucleic acids or polypeptides, may be used in any of the procedures described below.

**Genes Identified as Required for Proliferation of *Escherichia coli*, *Staphylococcus aureus*,  
15           *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Salmonella typhimurium*.**

          Genomic fragments were operably linked to an inducible promoter in a vector and assayed for growth inhibition activity. Example 1 describes the examination of a library of genomic fragments cloned into vectors comprising inducible promoters. Upon induction with xylose or IPTG, the vectors  
20           produced an RNA molecule corresponding to the subcloned genomic fragments. In those instances where the genomic fragments were in an antisense orientation with respect to the promoter, the transcript produced was complementary to at least a portion of an mRNA (messenger RNA) encoding a *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* or *Salmonella typhimurium* gene product such that they interacted with  
25           sense mRNA produced from various *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* or *Salmonella typhimurium* genes and thereby decreased the translation efficiency or the level of the sense messenger RNA thus decreasing production of the protein encoded by these sense mRNA molecules. In cases where the sense mRNA encoded a protein required for proliferation, bacterial cells containing a vector from which transcription  
30           from the promoter had been induced failed to grow or grew at a substantially reduced rate. Additionally, in cases where the transcript produced was complementary to at least a portion of a non-translated RNA and where that non-translated RNA was required for proliferation, bacterial cells containing a vector from which transcription from the promoter had been induced also failed to grow or grew at a substantially reduced rate. In contrast, cells grown under non-inducing conditions grow at a  
35           normal rate.

          The above method was used to identify genes required for cellular proliferation in *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Salmonella typhimurium*. Additionally, a number of genes required for cellular

proliferation in *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Salmonella typhimurium*, which have been described in the following U.S. Patent Applications: U.S. Patent Application Serial Number 09/492,709, filed January 27, 2000; U.S. Patent Application Serial Number 09/711,164, filed November 9, 2000; 5 U.S. Patent Application Serial Number 09/741,669, filed December 19, 2000 and U.S. Patent Application Serial Number 09/815,242 filed March 21, 2001, U.S. Provisional Patent Application Serial Number 60/342,923, filed October 25, 2001, have been previously identified using the above method.

### EXAMPLE 1

#### 10 Inhibition of Bacterial Proliferation after Induction of Antisense Expression

To identify genes required for proliferation of *E. coli*, random genomic fragments were cloned into the IPTG-inducible expression vector pLEX5BA (Krause et al., J. Mol. Biol. 274: 365 (1997) or a modified version of pLEX5BA, pLEX5BA-3' in which a synthetic linker containing a T7 terminator was ligated between the PstI and HindIII sites of pLEX5BA. In particular, to 15 construct pLEX5BA-3', the following oligonucleotides were annealed and inserted into the PstI and HindIII sites of pLEX5BA:

5' -GTCTAGCATAACCCCTTGGGGCCTCTAAACGGGTCCTTGAGGGGTTTTTTGA-3' (SEQ ID NO: 78584)  
 5' -AGCTTCAAAAAACCCCTCAAGGACCCGTTTAGAGGCCCAAGGGGTTAT  
 20 GCTAGACTGCA-3' (SEQ ID NO: 78585)

Random fragments of *E. coli* genomic DNA were generated by DNaseI digestion or sonication, filled in with T4 polymerase, and cloned into the SmaI site of pLEX5BA or pLEX5BA-3'. Upon activation or induction, the promoter transcribed the random genomic fragments.

A number of vectors which allow the production of transcripts which have an extended 25 lifetime in *E. coli* as well as other Gram negative bacteria can also be utilized in conjunction with these antisense inhibition experiments. Such vectors are described in U.S. Provisional Patent Application Serial Number 60/343,512, filed December 21, 2001. Briefly, the stabilized antisense RNA may comprise an antisense RNA which was identified as inhibiting proliferation as described above which has been engineered to contain at least one stem loop flanking each end of the 30 antisense nucleic acid. In some embodiments, the at least one stem-loop structure formed at the 5' end of the stabilized antisense nucleic acid comprises a flush, double stranded 5' end. In some embodiments, one or more of the stem loops comprises a rho independent terminator. In additional embodiments, the stabilized antisense RNA lacks a ribosome binding site. In further embodiments, the stabilized RNA lacks sites which are cleaved by one or more RNases, such as RNase E or 35 RNase III. In some embodiments, the stabilized antisense RNA may be transcribed in a cell which the activity of at least one enzyme involved in RNA degradation has been reduced. For example, the activity of an enzyme such as RNase E, RNase II, RNase III, polynucleotide phosphorylase, and poly(A) polymerase, RNA helicase, enolase or an enzyme having similar functions may be reduced in the cell.

To study the effects of transcriptional induction in liquid medium, growth curves were carried out by back diluting cultures 1:200 into fresh media with or without 1 mM IPTG and measuring the OD<sub>450</sub> every 30 minutes (min). To study the effects of transcriptional induction on solid medium, 10<sup>2</sup>, 10<sup>3</sup>, 10<sup>4</sup>, 10<sup>5</sup>, 10<sup>6</sup>, 10<sup>7</sup> and 10<sup>8</sup> fold dilutions of overnight cultures were prepared. Aliquots of from 0.5 to 3 µl of these dilutions were spotted on selective agar plates with or without 1 mM IPTG. After overnight incubation, the plates were compared to assess the sensitivity of the clones to IPTG.

Of the numerous clones tested, some clones were identified as containing a sequence that inhibited *E. coli* growth after IPTG induction. Accordingly, the gene to which the inserted nucleic acid sequence corresponds, or a gene within the operon containing the inserted nucleic acid, is required for proliferation in *E. coli*.

Nucleic acids involved in proliferation of *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Salmonella typhimurium* were identified as follows. Randomly generated fragments of *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* or *Salmonella typhimurium* genomic DNA were transcribed from inducible promoters.

In the case of *Staphylococcus aureus*, a novel inducible promoter system, XylT5, comprising a modified T5 promoter fused to the *xylO* operator from the *xylA* promoter of *Staphylococcus aureus* was used. The promoter is described in U.S. Patent Application Serial Number 10/032,393, filed December 21, 2001. Transcription from this hybrid promoter is inducible by xylose.

Randomly generated fragments of *Salmonella typhimurium* genomic DNA were transcribed from an IPTG inducible promoter in pLEX5BA (Krause et al., J. Mol. Biol. 274: 365 (1997) or a derivative thereof. Randomly generated fragments of *Klebsiella pneumoniae* genomic DNA were expressed from an IPTG inducible promoter in pLEX5BA-Kan. To construct pLEX5BA-kan, pLEX5BA was digested to completion with *ClaI* in order to remove the *bla* gene. Then the plasmid was treated with a partial *NotI* digestion and blunted with T4 DNA polymerase. A 3.2 kbp fragment was then gel purified and ligated to a blunted 1.3 kbp kan gene from pKan $\pi$ . Kan resistant transformants were selected on Kan plates. Orientation of the kan gene was checked by *SmaI* digestion. A clone, which had the kan gene in the same orientation as the *bla* gene, was used to identify genes required for proliferation of *Klebsiella pneumoniae*. Randomly generated fragments of *Pseudomonas aeruginosa* genomic DNA were transcribed from a two-component inducible promoter system. Integrated on the chromosome was the T7 RNA polymerase gene regulated by *lacUV5/ lacO* (Brunschwig, E. and Darzins, A. 1992. Gene 111:35-41. On a separate plasmid, a T7 gene 10 promoter, which is transcribed by T7 RNA polymerase, was fused with a *lacO* operator followed by a multiple cloning site.

Should the genomic DNA downstream of the promoter contain, in an antisense orientation, at least a portion of an mRNA or a non-translated RNA encoding a gene product involved in proliferation, then induction of transcription from the promoter will result in detectable inhibition of proliferation.

5 In the case of *Staphylococcus aureus*, a shotgun library of *Staphylococcus aureus* genomic fragments was cloned into the vector pXyIT5-P15a, which harbors the XyIT5 inducible promoter. The vector was linearized at a unique *Bam*HI site immediately downstream of the XyIT5 promoter/operator. The linearized vector was treated with shrimp alkaline phosphatase to prevent reclosure of the linearized ends. Genomic DNA isolated from *Staphylococcus aureus* strain RN450  
10 was fully digested with the restriction enzyme *Sau*3A, or, alternatively, partially digested with DNase I and "blunt-ended" by incubating with T4 DNA polymerase. Random genomic fragments between 200 and 800 base pairs in length were selected by gel purification. The size-selected genomic fragments were added to the linearized and dephosphorylated vector at a molar ratio of 0.1 to 1, and ligated to form a shotgun library.

15 The ligated products were transformed into electrocompetent *E. coli* strain XL1-Blue MRF' (Stratagene) and plated on LB medium with supplemented with carbenicillin at 100 µg/ml. Resulting colonies numbering  $5 \times 10^5$  or greater were scraped and combined, and were then subjected to plasmid purification.

The purified library was then transformed into electrocompetent *Staphylococcus aureus*  
20 RN4220. Resulting transformants were plated on agar containing LB + 0.2% glucose (LBG medium) + chloramphenicol at 15 µg/ml (LBG+CM15 medium) in order to generate 100 to 150 platings at 500 colonies per plating. The colonies were subjected to robotic picking and arrayed into wells of 384 well culture dishes. Each well contained 100µl of LBG + CM15 liquid medium. Inoculated 384 well dishes were incubated 16 hours at 37°C, and each well was robotically gridded  
25 onto solid LBG + CM15 medium with or without 2% xylose. Gridded plates were incubated 16 hours at 37°C, and then manually scored for arrayed colonies that were growth-compromised in the presence of xylose.

Arrayed colonies that were growth-sensitive on medium containing 2% xylose, yet were able to grow on similar medium lacking xylose, were subjected to further growth sensitivity  
30 analysis as follows: Colonies from the plate lacking xylose were manually picked and inoculated into individual wells of a 96 well culture dish containing LBG + CM15, and were incubated for 16 hours at 37°C. These cultures were robotically diluted 1/100 into fresh medium and allowed to incubate for 4 hours at 37°C, after which they were subjected to serial dilutions in a 384 well array and then gridded onto media containing 2% xylose or media lacking xylose. After growth for 16  
35 hours at 37°C, the arrays that resulted on the two media were compared to each other. Clones that grew similarly at all dilutions on both media were scored as a negative and were no longer considered. Clones that grew on xylose medium but failed to grow at the same serial dilution on the non-xylose plate were given a score based on the differential, i.e. should the clone grow at a

serial dilution of  $10^4$  or less on the xylose plate and grow at a serial dilution of  $10^8$  or less on the non-xylose plate, then the corresponding clone received a score of "4" representing the log difference in growth observed.

For *Salmonella typhimurium* and *Klebsiella pneumoniae* growth curves were carried out by back diluting cultures 1:200 into fresh media containing 1 mM IPTG or media lacking IPTG and measuring the OD<sub>450</sub> every 30 minutes (min). To study the effects of transcriptional induction on solid medium,  $10^2$ ,  $10^3$ ,  $10^4$ ,  $10^5$ ,  $10^6$ ,  $10^7$  and  $10^8$  fold dilutions of overnight cultures were prepared. Aliquots of from 0.5 to 3  $\mu$ l of these dilutions were spotted on selective agar plates with or without 1 mM IPTG. After overnight incubation, the plates were compared to assess the sensitivity of the clones to IPTG.

Nucleic acids involved in proliferation of *Pseudomonas aeruginosa* were identified as follows. Randomly generated fragments of *Pseudomonas aeruginosa* genomic DNA were transcribed from a two-component inducible promoter system. Integrated on the chromosome was the T7 RNA polymerase gene regulated by *lacUV5/ lacO* (Brunschwig, E. and Darzins, A. 1992. Gene 111:35-41). On an expression plasmid there was a T7 gene 10 promoter, which is transcribed by T7 RNA polymerase, fused with a *lacO* operator followed by a multiple cloning site. Transcription from this hybrid promoter is inducible by IPTG. Should the genomic DNA downstream of the promoter contain, in an antisense orientation, at least a portion of an mRNA encoding a gene product involved in proliferation, then induction of expression from the promoter will result in detectable inhibition of proliferation.

A shotgun library of *Pseudomonas aeruginosa* genomic fragments was cloned into the vectors pEP5, pEP5S, or other similarly constructed vectors which harbor the T7*lacO* inducible promoter. The vector was linearized at a unique *SmaI* site immediately downstream of the T7*lacO* promoter/operator. The linearized vector was treated with shrimp alkaline phosphatase to prevent reclosure of the linearized ends. Genomic DNA isolated from *Pseudomonas aeruginosa* strain PAO1 was partially digested with DNase I and "blunt-ended" by incubating with T4 DNA polymerase. Random genomic fragments between 200 and 800 base pairs in length were selected by gel purification. The size-selected genomic fragments were added to the linearized and dephosphorylated vector at a molar ratio of 2 to 1, and ligated to form a shotgun library.

The ligated products were transformed into electrocompetent *E. coli* strain XL1-Blue MRF' (Stratagene) and plated on LB medium with carbenicillin at 100  $\mu$ g/ml or Streptomycin 100  $\mu$ g/ml. Resulting colonies numbering  $5 \times 10^5$  or greater were scraped and combined, and were then subjected to plasmid purification.

The purified library was then transformed into electrocompetent *Pseudomonas aeruginosa* strain PAO1. Resulting transformants were plated on LB agar with carbenicillin at 100  $\mu$ g/ml or Streptomycin 40  $\mu$ g/ml in order to generate 100 to 150 platings at 500 colonies per plating. The colonies were subjected to robotic picking and arrayed into wells of 384 well culture dishes. Each well contained 100  $\mu$ l of LB + CB 100 or Streptomycin 40 liquid medium. Inoculated 384 well



dishes were incubated 16 hours at room temperature, and each well was robotically gridded onto solid LB + CB100 or Streptomycin 40 medium with or without 1 mM IPTG. Gridded plates were incubated 16 hours at 37°C, and then manually scored for arrayed colonies that were growth-compromised in the presence of IPTG.

5           Arrayed colonies that were growth-sensitive on medium containing 1 mM IPTG, yet were able to grow on similar medium lacking IPTG, were subjected to further growth sensitivity analysis as follows: Colonies from the plate lacking IPTG were manually picked and inoculated into individual wells of a 96 well culture dish containing LB + CB100 or Streptomycin 40, and were incubated for 16 hours at 30°C. These cultures were robotically diluted 1/100 into fresh medium  
10           and allowed to incubate for 4 hours at 37°C, after which they were subjected to serial dilutions in a 384 well array and then gridded onto media with and without 1 mM IPTG. After growth for 16 hours at 37°C, the arrays of serially diluted spots that resulted were compared between the two media. Clones that grew similarly at all dilutions on both media were scored as a negative and were no longer considered. Clones that grew on IPTG medium but failed to grow at the same serial  
15           dilution on the non-IPTG plate were given a score based on the differential, i.e. should the clone grow at a serial dilution of  $10^4$  or less on the IPTG plate and grow at a serial dilution of  $10^8$  or less on the IPTG plate, then the corresponding clone received a score of "4" representing the log difference in growth observed.

          Following the identification of those vectors that, upon induction, negatively impacted  
20           *Pseudomonas aeruginosa* growth or proliferation, the inserts or nucleic acid fragments contained in those vectors were isolated for subsequent characterization. Vectors of interest were subjected to nucleic acid sequence determination.

          Nucleic acids involved in proliferation of *E. faecalis* were identified as follows. Randomly generated fragments of genomic DNA were expressed from the vectors pEPEF3 or pEPEF14,  
25           which contain the CP25 or P59 promoter, respectively, regulated by the xyl operator/repressor. These plasmids as well as other vectors useful for the expression of nucleic acids in *Enterococcus faecalis* and other Gram positive organisms are described in U.S. Patent Application Serial Number 10/032,393, filed December 21, 2001, the disclosure of which is incorporated herein by reference in its entirety. Should the genomic DNA downstream of the promoter contain, in an antisense  
30           orientation, at least a portion of a mRNA encoding a gene product involved in proliferation, then induction of expression from the promoter will result in detectable inhibition of proliferation.

          A shotgun library of *E. faecalis* genomic fragments was cloned into the vector pEPEF3 or pEPEF14, which harbor xylose inducible promoters. The vector was linearized at a unique *Sma*I site immediately downstream of the promoter/operator. The linearized vector was treated with  
35           alkaline phosphatase to prevent reclosure of the linearized ends. Genomic DNA isolated from *E. faecalis* strain OG1RF was partially digested with DNase I and "blunt-ended" by incubating with T4 DNA polymerase. Random genomic fragments between 200 and 800 base pairs in length were

selected by gel purification. The size-selected genomic fragments were added to the linearized and dephosphorylated vector at a molar ratio of 2 to 1, and ligated to form a shotgun library.

The ligated products were transformed into electrocompetent *E. coli* strain TOP10 cells (Invitrogen) and plated on LB medium with erythromycin (Erm) at 150 µg/ml. Resulting colonies  
5 numbering  $5 \times 10^5$  or greater were scraped and combined, and were then subjected to plasmid purification.

The purified library was then transformed into electrocompetent *E. faecalis* strain OG1RF. Resulting transformants were plated on Todd-Hewitt (TH) agar with erythromycin at 10 µg/ml in order to generate 100 to 150 platings at 500 colonies per plating. The colonies were subjected to  
10 robotic picking and arrayed into wells of 384 well culture dishes. Each well contained 100 µl of THB + Erm 10 µg/ml. Inoculated 384 well dishes were incubated 16 hours at room temperature, and each well was robotically gridded onto solid TH agar + Erm with or without 5% xylose. Gridded plates were incubated 16 hours at 37°C, and then manually scored for arrayed colonies that were growth-compromised in the presence of xylose.

15 Arrayed colonies that were growth-sensitive on medium containing 5% xylose, yet were able to grow on similar medium lacking xylose, were subjected to further growth sensitivity analysis. Colonies from the plate lacking xylose were manually picked and inoculated into individual wells of a 96 well culture dish containing THB + Erm 10, and were incubated for 16 hours at 30°C. These cultures were robotically diluted 1/100 into fresh medium and allowed to  
20 incubate for 4 hours at 37°C, after which they were subjected to serial dilution on plates containing 5% xylose or plates lacking xylose. After growth for 16 hours at 37°C, the arrays of serially diluted spots that resulted were compared between the two media. Colonies that grew similarly on both media were scored as a negative and corresponding colonies were no longer considered. Colonies on xylose medium that failed to grow to the same serial dilution compared to those on the non-  
25 xylose plate were given a score based on the differential. For example, colonies on xylose medium that only grow to a serial dilution of -4 while they were able to grow to -8 on the non-xylose plate, then the corresponding transformant colony received a score of "4" representing the log difference in growth observed.

Following the identification of those vectors that, upon induction, negatively impacted *E.*  
30 *faecalis* growth or proliferation, the inserts or nucleic acid fragments contained in those expression vectors were isolated for subsequent characterization. The inserts in the vectors of interest were subjected to nucleotide sequence determination.

It will be appreciated that other restriction enzymes and other endonucleases or methodologies may be used to generate random genomic fragments. In addition, random genomic  
35 fragments may be generated by mechanical shearing. Sonication and nebulization are two such techniques commonly used for mechanical shearing of DNA.

## EXAMPLE 2

Nucleotide Sequence Determination of Identified Clones Transcribing Nucleic Acid Fragments with Detrimental Effects on *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* or *Salmonella typhimurium* Proliferation

5 Plasmids from clones that received a dilution plating score of "2" or greater were isolated to obtain the genomic DNA insert responsible for growth inhibition as follows.

The nucleotide sequences of the nucleic acid sequences which inhibited the growth of *Escherichia coli* were determined using plasmid DNA isolated using QIAPREP (Qiagen, Valencia, CA) and methods supplied by the manufacturer. The primers used for sequencing the inserts were 5' -  
10 TGTTTATCAGACCGCTT - 3' (SEQ ID NO: 78586) and 5' - ACAATTTACACAGCCTC - 3' (SEQ ID NO: 78587). These sequences flank the polylinker in pLEX5BA.

The nucleotide sequences of the nucleic acid sequences which inhibited the growth of *Staphylococcus aureus* were determined as follows. *Staphylococcus aureus* were grown in standard laboratory media (LB or TB with 15 ug/ml Chloramphenicol to select for the plasmid). Growth  
15 was carried out at 37°C overnight in culture tubes or 2 ml deep well microtiter plates.

Lysis of *Staphylococcus aureus* was performed as follows. Cultures (2-5 ml) were centrifuged and the cell pellets resuspended in 1.5 mg/ml solution of lysostaphin (20 µl/ml of original culture) followed by addition of 250 µl of resuspension buffer (Qiagen). Alternatively, cell pellets were resuspended directly in 250 µl of resuspension buffer (Qiagen) to which 5-20 µl of a 1  
20 mg/ml lysostaphin solution were added.

DNA was isolated using Qiagen miniprep kits or Wizard (Qiagen) miniprep kits according to the instructions provided by the manufacturer.

The genomic DNA inserts were amplified from the purified plasmids by PCR as follows.

1 µl of Qiagen purified plasmid was put into a total reaction volume of 25 µl Qiagen Hot  
25 Start PCR mix. For *Staphylococcus aureus*, the following primers were used in the PCR reaction:  
pXyITSF: CAGCAGTCTGAGTTATAAAATAG (SEQ ID NO: 78588)  
LexL TGTTTATCAGACCGCTT (SEQ ID NO: 78589)

Similar methods were conducted for *Salmonella typhimurium* and *Klebsiella pneumoniae*. For *Salmonella typhimurium* and *Klebsiella pneumoniae* the following primers were used:  
30 5' - TGTTTATCAGACCGCTT - 3' (SEQ ID NO: 78589) and  
5'-ACAATTTACACAGCCTC-3' (SEQ ID NO: 78587)

PCR was carried out in a PE GenAmp with the following cycle times:

- Step 1. 95° C 15 min
- Step 2. 94° C 45 sec
- 35 Step 3. 54° C 45 sec
- Step 4. 72° C 1 minute
- Step 5. Return to step 2, 29 times
- Step 6. 72° C 10 minutes

Step 7. 4° C hold

The PCR products were cleaned using Qiagen Qiaquick PCR plates according to the manufacturer's instructions.

For *Pseudomonas aeruginosa*, plasmids from transformant colonies that received a dilution  
5 plating score of "2" or greater were isolated to obtain the genomic DNA insert responsible for  
growth inhibition as follows. *Pseudomonas aeruginosa* were grown in standard laboratory media  
(LB with carbenicillin at 100 µg/ml or Streptomycin 40 µg/ml to select for the plasmid). Growth  
was carried out at 30°C overnight in 100 µl culture wells in microtiter plates. To amplify insert  
DNA 2 µl of culture were placed into 25 µl Qiagen Hot Start PCR mix. PCR reactions were in 96  
10 well microtiter plates. For plasmid pEP5S the following primers were used in the PCR reaction:

T7L1+: GTCGGCGATATAGGCGCCAGCAACCG (SEQ ID NO: 78590)

pStrA3: ATAATCGAGCATGAGTATCATACG (SEQ ID NO: 78591)

PCR was carried out in a PE GenAmp with the following cycle times:

Step 1. 95° C 15 min

15 Step 2. 94° C 45 sec

Step 3. 54° C 45 sec

Step 4. 72° C 1 minute

Step 5. Return to step 2, 29 times

Step 6. 72° C 10 minutes

20 Step 7. 4° C hold

The PCR products were cleaned using Qiagen Qiaquick PCR plates according to the manufacturer's instructions.

The purified PCR products were then directly cycle sequenced with Qiagen Hot Start PCR  
mix. The following primers were used in the sequencing reaction:

25 T7/L2: ATGCGTCCGGCGTAGAGGAT (SEQ ID NO: 78592)

PCR was carried out in a PE GenAmp with the following cycle times:

Step 1. 94° C 15 min

Step 2. 96° C 10 sec

Step 3. 50° C 5 sec

30 Step 4. 60 C 4 min

Step 5. Return to step 2, 24 times

Step 6. 4° C hold

The PCR products were cleaned using Qiagen Qiaquick PCR plates according to the manufacturer's instructions.

35 For *E. faecalis*, plasmids from transformant colonies that received a dilution plating score  
of "2" or greater were isolated to obtain the genomic DNA insert responsible for growth inhibition  
as follows. *E. faecalis* were grown in THB 10 µg/ml Erm at 30°C overnight in 100 µl culture wells

in microtiter plates. To amplify insert DNA 2  $\mu$ l of culture were placed into 25  $\mu$ l Qiagen Hot Start PCR mix. PCR reactions were in 96 well microtiter plates. The following primers were used in the PCR reaction:

pXylT5: CAGCAGTCTGAGTTATAAAATAG (SEQ ID NO: 78588) and the

5 pEP/pAK1 primer.

PCR was carried out in a PE GenAmp with the following cycle times:

Step 1. 95° C 15 min

Step 2. 94° C 45 sec

Step 3. 54° C 45 sec

10 Step 4. 72° C 1 minute

Step 5. Return to step 2, 29 times

Step 6. 72° C 10 minutes

Step 7. 4° C hold

The PCR products were cleaned using Qiagen Qiaquick PCR plates according to the manufacturer's

15 instructions.

The purified PCR products were then directly cycle sequenced with Qiagen Hot Start PCR mix. The following primers were used in the PCR reaction:

pXylT5: CAGCAGTCTGAGTTATAAAATAG (SEQ ID NO: 78588)

PCR was carried out in a PE GenAmp with the following cycle times:

20 Step 1. 94° C 15 min

Step 2. 96° C 10 sec

Step 3. 50° C 5 sec

Step 4. 60° C 4 min

Step 5. Return to step 2, 24 times

25 Step 6. 4° C hold

The PCR products were cleaned using Qiagen Qiaquick PCR plates according to the manufacturer's instructions.

The amplified genomic DNA inserts from each of the above procedures were subjected to automated sequencing. Sequence identification numbers (SEQ ID NOs) and clone names for the  
30 identified inserts are listed in Table IA and discussed below.

TABLE IA

SeqID	Clone Name	SeqID	Clone Name	SeqID	Clone Name	SeqID	Clone Name	SeqID	Clone Name
1	E3M10000001B01	1243	P33-1.C22	2485	E1M10000260G02	3727	P1M10000105C04	4969	S1M10000025G06
2	E3M10000001A02	1244	X3S107-17	2486	E1M10000260F04	3728	P1M10000105D04	4970	S1M10000025H06
3	E3M10000001B02	1245	P35-7	2487	E1M10000260A05	3729	P1M10000105C05	4971	S1M10000025H07
4	E3M10000001C02	1246	X3S118-9	2488	E1M10000260C05	3730	P1M10000105B06	4972	S1M10000025A08
5	E3M10000001D02	1247	X3S163-1	2489	E1M10000260E05	3731	P1M10000105C08	4973	S1M10000025D08
6	E3M10000001E02	1248	X3S204-7	2490	E1M10000260C07	3732	P1M10000105H08	4974	S1M10000025F08
7	E3M10000001F02	1249	X3S177-4	2491	E1M10000260G07	3733	P1M10000105D09	4975	S1M10000025H08
8	E3M10000001G02	1250	P342-3	2492	E1M10000260B08	3734	P1M10000110E01	4976	S1M10000025A09
9	E3M10000001H02	1251	SC21.1	2493	E1M10000260D08	3735	P1M10000110F01	4977	S1M10000025B09
10	E3M10000001E03	1252	SC17.1	2494	E1M10000260E08	3736	P1M10000110G01	4978	S1M10000025C09
11	E3M10000001G03	1253	SC13.1	2495	E1M10000260E09	3737	P1M10000110B02	4979	S1M10000025D09
12	E3M10000001H03	1254	MC9.6	2496	E1M10000260C10	3738	P1M10000110B03	4980	S1M10000025E09
13	E3M10000001D04	1255	Z60-P16	2497	E1M10000260D10	3739	P1M10000110F03	4981	S1M10000025F09
14	E3M10000001E04	1256	Z86-I21	2498	E1M10000260E10	3740	P1M10000110G03	4982	S1M10000025A10
15	E3M10000001F04	1257	E1M10000109A02	2499	E1M10000260G10	3741	P1M10000110D04	4983	S1M10000025C10
16	E3M10000001G04	1258	E1M10000109A11	2500	E1M10000260H10	3742	P1M10000110F04	4984	S1M10000025D10
17	E3M10000001H04	1259	E1M10000101F05	2501	E1M10000260H11	3743	P1M10000110B05	4985	S1M10000025F10
18	E3M10000001B05	1260	E1M10000101D06	2502	E1M10000260B12	3744	P1M10000110E05	4986	S1M10000025G10
19	E3M10000001D05	1261	E1M10000101A07	2503	E1M10000260D12	3745	P1M10000110B07	4987	S1M10000025H10
20	E3M10000001G05	1262	E1M10000101H07	2504	E1M10000260G12	3746	P1M10000110B08	4988	S1M10000025C11
21	E3M10000001A06	1263	E1M10000101H09	2505	E1M10000261F01	3747	P1M10000110F08	4989	S1M10000025E11
22	E3M10000001F06	1264	E1M10000101C12	2506	E1M10000261B02	3748	P1M10000110A09	4990	S1M10000025B12
23	E3M10000001B08	1265	E1M10000103B04	2507	E1M10000261H02	3749	P1M10000110E09	4991	S1M10000025F12
24	E3M10000001F08	1266	E1M10000103D11	2508	E1M10000261G04	3750	P1M10000110F09	4992	S1M10000026C01
25	E3M10000001C09	1267	E1M10000110G01	2509	E1M10000261H05	3751	P1M10000100F01	4993	S1M10000026E01
26	E3M10000001D09	1268	E1M10000110H01	2510	E1M10000261G06	3752	P1M10000098A02	4994	S1M10000026F01
27	E3M10000001E09	1269	E1M10000110E09	2511	E1M10000261H06	3753	P1M10000098B02	4995	S1M10000026G01
28	E3M10000001B10	1270	E1M10000110A12	2512	E1M10000261D08	3754	P1M10000098A03	4996	S1M10000026H01
29	E3M100000004D01	1271	E1M10000112F05	2513	E1M10000261F08	3755	P1M10000098D03	4997	S1M10000026A02
30	E3M100000004G01	1272	E1M10000113F02	2514	E1M10000261C09	3756	P1M10000098E04	4998	S1M10000026B02
31	E3M100000004D02	1273	E1M10000113A11	2515	E1M10000261H09	3757	P1M10000098G04	4999	S1M10000026H02
32	E3M100000004C03	1274	E1M10000111C03	2516	E1M10000261E10	3758	P1M10000098A05	5000	S1M10000026B03
33	E3M100000004A04	1275	E1M10000111E04	2517	E1M10000262E01	3759	P1M10000098C05	5001	S1M10000026F03

SeqID	Clone Name	SeqID	Clone Name	SeqID	Clone Name	SeqID	Clone Name	SeqID	Clone Name
34	E3M10000004F08	1276	E1M10000111F09	2518	E1M10000262C02	3760	P1M10000098G06	5002	S1M10000026G03
35	E3M10000004D10	1277	E1M10000115H01	2519	E1M10000262E02	3761	P1M10000098H06	5003	S1M10000026H03
36	E3M10000004F10	1278	E1M10000115G02	2520	E1M10000262F02	3762	P1M10000098C07	5004	S1M10000026A04
37	E3M10000004E11	1279	E1M10000115E03	2521	E1M10000262D03	3763	P1M10000098F07	5005	S1M10000026D04
38	E3M10000004H11	1280	E1M10000115G04	2522	E1M10000262G04	3764	P1M10000098A08	5006	S1M10000026F04
39	E3M10000005B01	1281	E1M10000115C06	2523	E1M10000262C05	3765	P1M10000098G08	5007	S1M10000026G04
40	E3M10000005C01	1282	E1M10000116B01	2524	E1M10000262A06	3766	P1M10000098H09	5008	S1M10000026H04
41	E3M10000005E01	1283	E1M10000106D02	2525	E1M10000262A07	3767	P1M10000098B11	5009	S1M10000026A05
42	E3M10000005E02	1284	E1M10000106G02	2526	E1M10000262E07	3768	P1M10000098C12	5010	S1M10000026B05
43	E3M10000005C03	1285	E1M10000106E04	2527	E1M10000262E08	3769	P1M10000099D01	5011	S1M10000026D05
44	E3M10000005D03	1286	E1M10000106F05	2528	E1M10000262B10	3770	P1M10000099G03	5012	S1M10000026F05
45	E3M10000005E03	1287	E1M10000106H05	2529	E1M10000262H10	3771	P1M10000099A09	5013	S1M10000026G05
46	E3M10000005C04	1288	E1M10000106H06	2530	E1M10000262G11	3772	P1M10000099A10	5014	S1M10000026H05
47	E3M10000005D04	1289	E1M10000106A08	2531	E1M10000262D12	3773	P1M10000099E10	5015	S1M10000026A06
48	E3M10000005H04	1290	E1M10000106E09	2532	E1M10000262G12	3774	P1M10000099F10	5016	S1M10000026B06
49	E3M10000005G05	1291	E1M10000106G10	2533	E1M10000263F01	3775	P1M10000099D11	5017	S1M10000026C06
50	E3M10000005A07	1292	E1M10000106D11	2534	E1M10000263H05	3776	P1M10000106D02	5018	S1M10000026D06
51	E3M10000005F07	1293	E1M10000122B03	2535	E1M10000263C06	3777	P1M10000106F03	5019	S1M10000026F06
52	E3M10000005B08	1294	E1M10000123D05	2536	E1M10000263G06	3778	P1M10000106H03	5020	S1M10000026G06
53	E3M10000005E08	1295	E1M10000123C09	2537	E1M10000263B07	3779	P1M10000106F04	5021	S1M10000026A07
54	E3M10000005D10	1296	E1M10000123E09	2538	E1M10000263F08	3780	P1M10000106D05	5022	S1M10000026B07
55	E3M10000005F10	1297	E1M10000123H10	2539	E1M10000263A10	3781	P1M10000106E07	5023	S1M10000026C07
56	E3M10000006C01	1298	E1M10000123F11	2540	E1M10000263A11	3782	P1M10000107E02	5024	S1M10000026D07
57	E3M10000006G02	1299	E1M10000107B02	2541	E1M10000263H11	3783	P1M10000107H02	5025	S1M10000026F07
58	E3M10000006B03	1300	E1M10000107E02	2542	E1M10000263C12	3784	P1M10000107C03	5026	S1M10000026G07
59	E3M10000006D03	1301	E1M10000107G02	2543	E1M10000263D12	3785	P1M10000107A04	5027	S1M10000026H07
60	E3M10000006F04	1302	E1M10000107B03	2544	E1M10000264B02	3786	P1M10000107C04	5028	S1M10000026A08
61	E3M10000006G04	1303	E1M10000107C03	2545	E1M10000264C02	3787	P1M10000107C09	5029	S1M10000026C08
62	E3M10000006H09	1304	E1M10000107H04	2546	E1M10000264F02	3788	P1M10000107C10	5030	S1M10000026D08
63	E3M10000006E11	1305	E1M10000107G08	2547	E1M10000264D03	3789	P1M10000107D10	5031	S1M10000026F08
64	E3M10000006C12	1306	E1M10000107F09	2548	E1M10000264F03	3790	P1M10000107H10	5032	S1M10000026G08
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67	E3M10000007G01	1309	E1M10000118C04	2551	E1M10000264C04	3793	P1M10000108B02	5035	S1M10000026G09
68	E3M10000007A02	1310	E1M10000118B05	2552	E1M10000264E04	3794	P1M10000108A03	5036	S1M10000026H09
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73	E3M10000007H03	1315	E1M10000119A04	2557	E1M10000264D11	3799	P1M10000108F06	5041	S1M10000026F10
74	E3M10000007C04	1316	E1M10000131H01	2558	E1M10000264F11	3800	P1M10000108G06	5042	S1M10000026G10
75	E3M10000007E05	1317	E1M10000131F04	2559	E1M10000264H11	3801	P1M10000109A02	5043	S1M10000026H10
76	E3M10000007F06	1318	E1M10000131C06	2560	E1M10000264B12	3802	P1M10000109C03	5044	S1M10000026A11
77	E3M10000008E02	1319	E1M10000131B07	2561	E1M10000264C12	3803	P1M10000109E03	5045	S1M10000026B11
78	E3M10000008H02	1320	E1M10000131C07	2562	E1M10000265A02	3804	P1M10000109D04	5046	S1M10000026C11
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80	E3M10000008G05	1322	E1M10000131G10	2564	E1M10000265G02	3806	P1M10000109B08	5048	S1M10000026B12
81	E3M10000008C08	1323	E1M10000135B02	2565	E1M10000265D04	3807	P1M10000109H09	5049	S1M10000026C12
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83	E3M10000008C09	1325	E1M10000132F02	2567	E1M10000265E05	3809	P1M10000109F10	5051	S1M10000026E12
84	E3M10000008G09	1326	E1M10000132H04	2568	E1M10000265H05	3810	P1M10000109E11	5052	S1M10000026F12
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86	E3M10000009E02	1328	E1M10000133A06	2570	E1M10000265E09	3812	S4M10000001C01	5054	S1M10000027G01
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93	E3M10000010F01	1335	E1M10000144B06	2577	E1M10000266H02	3819	S4M10000009E03	5061	S1M10000027E03
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103	E3M10000011C07	1345	E1M10000124G03	2587	E1M10000267A07	3829	S4M10000010D07	5071	S1M10000027F05
104	E3M10000011A09	1346	E1M10000124G04	2588	E1M10000267H07	3830	S4M10000010D08	5072	S1M10000027G05
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108	E3M10000012B02	1350	E1M10000125A02	2592	E1M10000267A10	3834	S4M10000010D10	5076	S1M10000027D06
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113	E3M10000012F07	1355	E1M10000120E05	2597	E1M10000267E12	3839	S4M10000011F10	5081	S1M10000027B07
114	E3M10000012G07	1356	E1M10000120A06	2598	E1M10000268F03	3840	S4M10000011F10	5082	S1M10000027D07
115	E3M10000012B08	1357	E1M10000120F06	2599	E1M10000268D04	3841	S4M10000011D11	5083	S1M10000027E07
116	E3M10000012D10	1358	E1M10000120A10	2600	E1M10000268E04	3842	S4M10000012H03	5084	S1M10000027G07
117	E3M10000012F10	1359	E1M10000120G10	2601	E1M10000268F06	3843	S4M10000012B06	5085	S1M10000027H07
118	E3M10000013D02	1360	E1M10000136C01	2602	E1M10000268E07	3844	S4M10000012B12	5086	S1M10000027A08
119	E3M10000013E02	1361	E1M10000136H01	2603	E1M10000268A08	3845	S4M10000013D02	5087	S1M10000027B08
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126	E3M10000013D08	1368	E1M10000121E07	2610	E1M10000268G09	3852	S4M10000016A02	5094	S1M10000027B09
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128	E3M10000013D10	1370	E1M10000129G04	2612	E1M10000268A11	3854	S4M10000021E07	5096	S1M10000027D09
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131	E3M10000014B12	1373	E1M10000126E08	2615	E1M10000269D01	3857	S4M10000022B05	5099	S1M10000027G09
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136	E3M10000016A03	1378	E1M10000137C03	2620	E1M10000269B05	3862	S4M10000024G04	5104	S1M10000027B11
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139	E3M10000016G05	1381	E1M10000137B08	2623	E1M10000269A06	3865	S4M10000024G09	5107	S1M10000027G11
140	E3M10000016H05	1382	E1M10000137G09	2624	E1M10000269E07	3866	S4M10000024C11	5108	S1M10000027H11
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146	E3M10000018E01	1388	E1M10000142H03	2630	E1M10000271F02	3872	S4M10000026C01	5114	S1M10000028B02
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174	E3M10000022C05	1416	E1M10000152H08	2658	E1M10000272G09	3900	S4M10000036H11	5142	S1M10000028D07
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176	E3M10000022C06	1418	E1M10000153H03	2660	E1M10000273E01	3902	S4M10000037A08	5144	S1M10000028H07
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180	E3M10000022F08	1422	E1M10000153A09	2664	E1M10000273E05	3906	S4M10000033G05	5148	S1M10000028D08
181	E3M10000022C09	1423	E1M10000156D07	2665	E1M10000273G05	3907	S4M10000033F08	5149	S1M10000028E08
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198	E3M10000023A07	1440	E1M10000160B09	2682	E1M10000274F09	3924	S1M10000001E09	5166	S1M10000029C03
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200	E3M10000023C08	1442	E1M10000160E09	2684	E1M10000274D11	3926	S1M10000001A10	5168	S1M10000029A04
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203	E3M10000023C09	1445	E1M10000160F11	2687	E1M10000275C01	3929	S1M10000001E11	5171	S1M10000029G04
204	E3M10000023E09	1446	E1M10000162C01	2688	E1M10000275E01	3930	S1M10000002B01	5172	S1M10000029B05
205	E3M10000023F10	1447	E1M10000162A03	2689	E1M10000275B02	3931	S1M10000002D01	5173	S1M10000029C05
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253	E3M10000027G08	1495	E1M10000169H02	2737	E1M10000313A02	3979	S1M10000003G04	5221	S1M10000030A05
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284	E3M10000028D06	1526	E1M10000187F11	2768	E1M10000314G10	4010	S1M10000004F02	5252	S1M10000030G11
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352	E3M10000029F12	1594	E1M10000194H07	2836	E1M10000279H07	4078	S1M10000005A11	5320	S1M10000032B05
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354	E3M10000030E01	1596	E1M10000194G08	2838	E1M10000279A09	4080	S1M10000005D11	5322	S1M10000032F05
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356	E3M10000030G01	1598	E1M10000194B10	2840	E1M10000279C10	4082	S1M10000005B12	5324	S1M10000032A06
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362	E3M10000030H03	1604	E1M10000195B03	2846	E1M10000280C03	4088	S1M10000006G02	5330	S1M10000032C07
363	E3M10000030B04	1605	E1M10000195G03	2847	E1M10000280C05	4089	S1M10000006A03	5331	S1M10000032D07
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366	E3M10000030F04	1608	E1M10000195D06	2850	E1M10000280B06	4092	S1M10000006E03	5334	S1M10000032A08
367	E3M10000030H04	1609	E1M10000195E07	2851	E1M10000280H06	4093	S1M10000006F03	5335	S1M10000032B08
368	E3M10000030A05	1610	E1M10000195A08	2852	E1M10000280A07	4094	S1M10000006G03	5336	S1M10000032D08
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370	E3M10000030D05	1612	E1M10000195D10	2854	E1M10000280G07	4096	S1M10000006B04	5338	S1M10000032G08
371	E3M10000030E05	1613	E1M10000195E10	2855	E1M10000280E08	4097	S1M10000006C04	5339	S1M10000032B09
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373	E3M10000030D06	1615	E1M10000195F11	2857	E1M10000280C09	4099	S1M10000006F04	5341	S1M10000032D09
374	E3M10000030F06	1616	E1M10000196B02	2858	E1M10000280H09	4100	S1M10000006G04	5342	S1M10000032E09
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376	E3M10000030H06	1618	E1M10000196E02	2860	E1M10000280C11	4102	S1M10000006D05	5344	S1M10000032A10
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387	E3M10000030D09	1629	E1M10000196H07	2871	E1M10000281B10	4113	S1M10000006G07	5355	S1M10000032H11
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389	E3M10000030G09	1631	E1M10000196A10	2873	E1M10000281G11	4115	S1M10000006E08	5357	S1M10000032C12
390	E3M10000030B10	1632	E1M10000196B10	2874	E1M10000281D12	4116	S1M10000006A10	5358	S1M10000032E12
391	E3M10000030D10	1633	E1M10000196D11	2875	E1M10000281F12	4117	S1M10000006B10	5359	S1M10000032F12
392	E3M10000030E10	1634	E1M10000196D12	2876	E1M10000282D01	4118	S1M10000006C10	5360	S1M10000032G12
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396	E3M10000030B11	1638	E1M10000197D04	2880	E1M10000282F03	4122	S1M10000006A12	5364	S1M10000033D02
397	E3M10000030H11	1639	E1M10000197B05	2881	E1M10000282C04	4123	S1M10000006B12	5365	S1M10000033F02
398	E3M10000030B12	1640	E1M10000197E07	2882	E1M10000282E04	4124	S1M10000007F01	5366	S1M10000033H02
399	E3M10000030C12	1641	E1M10000197E08	2883	E1M10000282F04	4125	S1M10000007B02	5367	S1M10000033D03
400	E3M10000030D12	1642	E1M10000197H08	2884	E1M10000282H04	4126	S1M10000007F02	5368	S1M10000033F03
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403	E3M10000031C01	1645	E1M10000197E10	2887	E1M10000282H05	4129	S1M10000007D03	5371	S1M10000033D04
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409	E3M10000031E03	1651	E1M10000197B12	2893	E1M10000282G08	4135	S1M10000007G05	5377	S1M10000033A07
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424	E3M10000031E07	1666	E1M10000199F02	2908	E1M10000283B05	4150	S1M10000008F01	5392	S1M10000033H10
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428	E3M10000031A08	1670	E1M10000199C06	2912	E1M10000283A07	4154	S1M10000008B03	5396	S1M10000033H11
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432	E3M10000031B09	1674	E1M10000199G09	2916	E1M10000283F08	4158	S1M10000008B04	5400	S1M10000033G12
433	E3M10000031E09	1675	E1M10000199H09	2917	E1M10000283B10	4159	S1M10000008D05	5401	S1M10000034B01
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446	E3M10000032D01	1688	E1M10000200A03	2930	E1M10000303A02	4172	S1M10000008E09	5414	S1M10000034G03
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450	E3M10000032C02	1692	E1M10000200C07	2934	E1M10000303H03	4176	S1M10000008F10	5418	S1M10000034F04
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452	E3M10000032F02	1694	E1M10000200D08	2936	E1M10000303B05	4178	S1M10000008B01	5420	S1M10000034B05
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463	E3M10000032E05	1705	E1M10000201G06	2947	E1M10000304A03	4189	S1M10000008F02	5431	S1M10000034B07
464	E3M10000032F05	1706	E1M10000201H07	2948	E1M10000304C03	4190	S1M10000008G02	5432	S1M10000034C07
465	E3M10000032G05	1707	E1M10000201G08	2949	E1M10000304E03	4191	S1M10000008H02	5433	S1M10000034D07

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468	E3M10000032C06	1710	E1M10000201H09	2952	E1M10000304G05	4194	S1M10000009F03	5436	S1M10000034G07
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471	E3M10000032H06	1713	E1M10000201F12	2955	E1M10000304A08	4197	S1M10000009A04	5439	S1M10000034B08
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474	E3M10000032G07	1716	E1M10000202C08	2958	E1M10000305C02	4200	S1M10000009B05	5442	S1M10000034G08
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485	E3M10000032H10	1727	E1M10000203C12	2969	E1M10000306C05	4211	S1M10000009A07	5453	S1M10000034F10
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487	E3M10000032B11	1729	E1M10000204F02	2971	E1M10000306D09	4213	S1M10000009C07	5455	S1M10000034A11
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490	E3M10000032F11	1732	E1M10000204B05	2974	E1M10000307G01	4216	S1M10000009G07	5458	S1M10000034G11
491	E3M10000032B12	1733	E1M10000204A06	2975	E1M10000307C02	4217	S1M10000009H07	5459	S1M10000034A12
492	E3M10000032C12	1734	E1M10000204A07	2976	E1M10000307D02	4218	S1M10000009A08	5460	S1M10000034B12
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496	E3M10000033B01	1738	E1M10000204H10	2980	E1M10000307E04	4222	S1M10000009C09	5464	S1M10000034F12
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536	E3M10000033F08	1778	E1M10000208F08	3020	E1M10000286D01	4262	S1M10000011A04	5504	S1M10000035E12
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554	E3M10000033C12	1796	E1M10000210G05	3038	E1M10000286H08	4280	S1M10000012G01	5522	S1M10000036B06
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576	E3M10000035B01	1818	E1M10000213G07	3060	E1M10000287A10	4302	S1M10000012E07	5544	S1M10000036C10
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678	E3M10000036C09	1920	E1M10000216E07	3162	E1M10000293D12	4404	S1M10000014B05	5646	S1M10000038B08
679	E3M10000036D09	1921	E1M10000216A09	3163	E1M10000295D01	4405	S1M10000014C05	5647	S1M10000038C08
680	E3M10000036F09	1922	E1M10000216B10	3164	E1M10000295G01	4406	S1M10000014E05	5648	S1M10000038D08
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684	E3M10000036D10	1926	E1M10000216D12	3168	E1M10000295H04	4410	S1M10000014C06	5652	S1M10000038B09
685	E3M10000036F10	1927	E1M10000217D02	3169	E1M10000295A07	4411	S1M10000014D06	5653	S1M10000038D09
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687	E3M10000036H10	1929	E1M10000217H02	3171	E1M10000295C07	4413	S1M10000014H06	5655	S1M10000038H09
688	E3M10000036B11	1930	E1M10000217C04	3172	E1M10000295D08	4414	S1M10000014A07	5656	S1M10000038C10
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690	E3M10000036D11	1932	E1M10000217B07	3174	E1M10000295G08	4416	S1M10000014C07	5658	S1M10000038E10
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714	E3M10000037H05	1956	E1M10000219C01	3198	E1M10000296H07	4440	S1M10000014B12	5682	S1M10000039G03
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720	E3M10000037B07	1962	E1M10000219C06	3204	E1M10000296B11	4446	S1M10000015G01	5688	S1M10000039F05
721	E3M10000037C07	1963	E1M10000219G07	3205	E1M10000296E11	4447	S1M10000015A02	5689	S1M10000039H05
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762	E3M10000038E05	2004	E1M10000222E12	3246	E1M10000311E11	4488	S1M10000015B10	5730	S1M10000040B03
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766	E3M10000038F06	2008	E1M10000223H11	3250	E1M10000292D08	4492	S1M10000015G10	5734	S1M10000040G03
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775	E3M10000038H07	2017	E1M10000225A06	3259	E1M10000294F04	4501	S1M10000016C01	5743	S1M10000040C05
776	E3M10000038A08	2018	E1M10000225B06	3260	E1M10000294H04	4502	S1M10000016D01	5744	S1M10000040D05
777	E3M10000038B08	2019	E1M10000225B07	3261	E1M10000294D05	4503	S1M10000016G01	5745	S1M10000040E05
778	E3M10000038D08	2020	E1M10000225E08	3262	E1M10000294F05	4504	S1M10000016B02	5746	S1M10000040F05
779	E3M10000038E08	2021	E1M10000225E09	3263	E1M10000294H05	4505	S1M10000016C02	5747	S1M10000040H05
780	E3M10000038H08	2022	E1M10000225H09	3264	E1M10000294C06	4506	S1M10000016D02	5748	S1M10000040C06
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784	E3M10000038H09	2026	E1M10000226E01	3268	E1M10000294B09	4510	S1M10000016G03	5752	S1M10000040B07
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786	E3M10000038C10	2028	E1M10000226C02	3270	E1M10000294F09	4512	S1M10000016A04	5754	S1M10000040E07
787	E3M10000038D10	2029	E1M10000226F02	3271	E1M10000294B10	4513	S1M10000016C04	5755	S1M10000040G07
788	E3M10000038F10	2030	E1M10000226D03	3272	E1M10000294G10	4514	S1M10000016D04	5756	S1M10000040H07
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795	E3M10000038G11	2037	E1M10000226D09	3279	E1M10000300G09	4521	S1M10000016E05	5763	S1M10000040H08
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824	E3M10000039F06	2066	E1M10000232G08	3308	E1M10000309F12	4550	S1M10000016H10	5792	S1M10000041B06
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925	E3M10000041G06	2167	E1M10000239H05	3409	K1M10000003C01	4651	S1M10000018B11	5893	S1M10000043B09
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927	E3M10000041A07	2169	E1M10000239A08	3411	K1M10000007F01	4653	S1M10000018D11	5895	S1M10000043G09
928	E3M10000041C07	2170	E1M10000239D08	3412	K1M10000008C10	4654	S1M10000018E11	5896	S1M10000043H09
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930	E3M10000041F07	2172	E1M10000239H08	3414	K1M10000013E06	4656	S1M10000018C12	5898	S1M10000043B10
931	E3M10000041G07	2173	E1M10000239H10	3415	K1M10000015E05	4657	S1M10000018D12	5899	S1M10000043D10
932	E3M10000041A08	2174	E1M10000239G11	3416	K1M10000019D06	4658	S1M10000018E12	5900	S1M10000043E10
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936	E3M10000041F08	2178	E1M10000240A04	3420	K1M10000030C04	4662	S1M10000019C01	5904	S1M10000043C11
937	E3M10000041G08	2179	E1M10000240D06	3421	K1M10000030C07	4663	S1M10000019D01	5905	S1M10000043E11
938	E3M10000041H08	2180	E1M10000240G07	3422	K1M10000030E07	4664	S1M10000019E01	5906	S1M10000043H11
939	E3M10000041A09	2181	E1M10000240C08	3423	K1M10000032E11	4665	S1M10000019F01	5907	S1M10000043A12
940	E3M10000041B09	2182	E1M10000240F08	3424	K1M10000033E01	4666	S1M10000019A02	5908	S1M10000043B12
941	E3M10000041C09	2183	E1M10000240B10	3425	K1M10000033B02	4667	S1M10000019D02	5909	S1M10000043C12
942	E3M10000041D09	2184	E1M10000240H11	3426	K1M10000037D10	4668	S1M10000019E02	5910	S1M10000043D12
943	E3M10000041F09	2185	E1M10000240H11	3427	K1M10000038D04	4669	S1M10000019A03	5911	S1M10000043E12
944	E3M10000041G09	2186	E1M10000240B12	3428	K1M10000039A12	4670	S1M10000019B03	5912	S1M10000044B01
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963	E3M10000041D12	2205	E1M10000242H07	3447	P1M10000024D06	4689	S1M10000019E07	5931	S1M10000044H06
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965	E3M10000042B01	2207	E1M10000242E11	3449	P1M10000025G07	4691	S1M10000019A08	5933	S1M10000044E07
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967	E3M10000042G01	2209	E1M10000242E12	3451	P1M10000026H02	4693	S1M10000019C08	5935	S1M10000044A08
968	E3M10000042A02	2210	E1M10000243F03	3452	P1M10000026F04	4694	S1M10000019F08	5936	S1M10000044B08
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972	E3M10000042A03	2214	E1M10000243F06	3456	P1M10000026G09	4698	S1M10000019B09	5940	S1M10000044G08
973	E3M10000042C03	2215	E1M10000243F07	3457	P1M10000027B02	4699	S1M10000019D09	5941	S1M10000044H08
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978	E3M10000042G05	2220	E1M10000244F01	3462	P1M10000028A08	4704	S1M10000019A11	5946	S1M10000044D10
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981	E3M10000042G07	2223	E1M10000244H02	3465	P1M10000029A09	4707	S1M10000019F11	5949	S1M10000044G10
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985	E3M10000042H08	2227	E1M10000244A04	3469	P1M10000033E03	4711	S1M10000019C12	5953	S1M10000044C11
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999	E3M10000042F12	2241	E1M10000245C01	3483	P1M10000040C01	4725	S1M10000020A05	5967	S1M10000045B03
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1002	E3M10000043C01	2244	E1M10000245H03	3486	P1M10000040D04	4728	S1M10000020G05	5970	S1M10000045G03
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1004	E3M10000043A02	2246	E1M10000245B04	3488	P1M10000040E10	4730	S1M10000020B06	5972	S1M10000045E04
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1009	E3M10000043B03	2251	E1M10000245F06	3493	P1M10000042E08	4735	S1M10000020A07	5977	S1M10000045A06
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1018	E3M10000043B06	2260	E1M10000245B12	3502	P1M10000046C09	4744	S1M10000020H08	5986	S1M10000045D08
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1020	E3M10000043H06	2262	E1M10000245E12	3504	P1M10000047H02	4746	S1M10000020C09	5988	S1M10000045F08
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1039	E3M10000043F10	2281	E1M10000247G01	3523	P1M10000055C08	4765	S1M10000021E01	6007	S1M10000045D12
1040	E3M10000043G10	2282	E1M10000247E02	3524	P1M10000055A11	4766	S1M10000021G01	6008	S1M10000045E12
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1050	E3M10000044E01	2292	E1M10000247G07	3534	P1M10000062H01	4776	S1M10000021H04	6018	S1M10000046D02
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1062	E3M10000050C02	2304	E1M10000248G06	3546	P1M10000063F02	4788	S1M10000021G06	6030	S1M10000046E04
1063	E3M10000050E02	2305	E1M10000248H08	3547	P1M10000063G02	4789	S1M10000021A07	6031	S1M10000046G04
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1066	E3M10000050B05	2308	E1M10000249G01	3550	P1M10000064C03	4792	S1M10000021F07	6034	S1M10000046D05
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1068	E3M10000050E05	2310	E1M10000249F02	3552	P1M10000064E05	4794	S1M10000021A08	6036	S1M10000046A06
1069	E3M10000050G05	2311	E1M10000249F03	3553	P1M10000064H07	4795	S1M10000021C08	6037	S1M10000046C06
1070	E3M10000050H05	2312	E1M10000249H04	3554	P1M10000064A10	4796	S1M10000021G08	6038	S1M10000046F06
1071	E3M10000050A06	2313	E1M10000249G05	3555	P1M10000064G12	4797	S1M10000021H08	6039	S1M10000046B07
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1074	E3M10000050F06	2316	E1M10000249A07	3558	P1M10000065A04	4800	S1M10000021E09	6042	S1M10000046G07
1075	E3M10000050H06	2317	E1M10000249C07	3559	P1M10000065C05	4801	S1M10000021F09	6043	S1M10000046A08
1076	E3M10000050A07	2318	E1M10000249B08	3560	P1M10000065D06	4802	S1M10000021A10	6044	S1M10000046B08
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1080	E3M10000050F07	2322	E1M10000249H09	3564	P1M10000066F04	4806	S1M10000021C11	6048	S1M10000046F08
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1083	E3M10000050D08	2325	E1M10000249H11	3567	P1M10000067C01	4809	S1M10000021C12	6051	S1M10000046D09
1084	E3M10000050F08	2326	E1M10000250F02	3568	P1M10000067E01	4810	S1M10000021B12	6052	S1M10000046F09
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1086	E3M10000050D09	2328	E1M10000250E03	3570	P1M10000067A05	4812	S1M10000022E01	6054	S1M10000046D10
1087	E3M10000050F09	2329	E1M10000250G03	3571	P1M10000067D05	4813	S1M10000022A02	6055	S1M10000046E10
1088	E3M10000050G09	2330	E1M10000250A04	3572	P1M10000067F05	4814	S1M10000022B02	6056	S1M10000046F10
1089	E3M10000050H09	2331	E1M10000250E04	3573	P1M10000067G05	4815	S1M10000022C02	6057	S1M10000046G10
1090	E3M10000050B10	2332	E1M10000250H04	3574	P1M10000067A06	4816	S1M10000022A03	6058	S1M10000046H10
1091	E3M10000051C01	2333	E1M10000250A05	3575	P1M10000067C06	4817	S1M10000022B03	6059	S1M10000046A11
1092	E3M10000051D01	2334	E1M10000250E05	3576	P1M10000067A08	4818	S1M10000022C03	6060	S1M10000046B11
1093	E3M10000051C03	2335	E1M10000250G07	3577	P1M10000068G01	4819	S1M10000022D03	6061	S1M10000046C11
1094	E3M10000051D03	2336	E1M10000250D09	3578	P1M10000068D04	4820	S1M10000022E03	6062	S1M10000046D11
1095	E3M10000051H03	2337	E1M10000250G09	3579	P1M10000068F04	4821	S1M10000022G03	6063	S1M10000046A12
1096	E3M10000051A04	2338	E1M10000250B10	3580	P1M10000068H05	4822	S1M10000022H03	6064	S1M10000046B12
1097	E3M10000051B04	2339	E1M10000250E10	3581	P1M10000068F08	4823	S1M10000022C04	6065	S1M10000046C12
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1102	E3M10000051C06	2344	E1M10000251D04	3586	P1M10000069D09	4828	S1M10000022D05	6070	S1M10000047E01
1103	E3M10000051D06	2345	E1M10000251F04	3587	P1M10000070E03	4829	S1M10000022E05	6071	S1M10000047G01
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1106	E3M10000051B07	2348	E1M10000251A07	3590	P1M10000070G06	4832	S1M10000022C06	6074	S1M10000047D02
1107	E3M10000051E07	2349	E1M10000251C07	3591	P1M10000070H06	4833	S1M10000022D06	6075	S1M10000047E02
1108	E3M10000051F07	2350	E1M10000251B08	3592	P1M10000070D08	4834	S1M10000022F06	6076	S1M10000047F02
1109	E3M10000051A08	2351	E1M10000251H08	3593	P1M10000070B10	4835	S1M10000022H06	6077	S1M10000047G02
1110	E3M10000051B08	2352	E1M10000251H09	3594	P1M10000070G12	4836	S1M10000022B07	6078	S1M10000047A03
1111	E3M10000051D08	2353	E1M10000251C10	3595	P1M10000071B01	4837	S1M10000022C07	6079	S1M10000047C03
1112	E3M10000051H08	2354	E1M10000251F11	3596	P1M10000071C01	4838	S1M10000022D07	6080	S1M10000047D03
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1115	E3M10000051D09	2357	E1M10000251D12	3599	P1M10000071E04	4841	S1M10000022H07	6083	S1M10000047G03		
1116	E3M10000051E09	2358	E1M10000251F12	3600	P1M10000073G03	4842	S1M10000022A08	6084	S1M10000047H03		
1117	E3M10000051G09	2359	E1M10000252D01	3601	P1M10000073D04	4843	S1M10000022B08	6085	S1M10000047A04		
1118	E3M10000051H09	2360	E1M10000252G02	3602	P1M10000073A06	4844	S1M10000022C08	6086	S1M10000047B04		
1119	E3M10000051A10	2361	E1M10000252C03	3603	P1M10000073D09	4845	S1M10000022D08	6087	S1M10000047C04		
1120	E3M10000051B10	2362	E1M10000252G03	3604	P1M10000073B10	4846	S1M10000022F08	6088	S1M10000047D04		
1121	E3M10000051D10	2363	E1M10000252B04	3605	P1M10000074B01	4847	S1M10000022G08	6089	S1M10000047E04		
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1127	E3M10000051E11	2369	E1M10000252A07	3611	P1M10000075F02	4853	S1M10000022C11	6095	S1M10000047C05		
1128	E3M10000051F11	2370	E1M10000252H07	3612	P1M10000075B03	4854	S1M10000022D11	6096	S1M10000047D05		
1129	E3M10000051G11	2371	E1M10000252A09	3613	P1M10000075A04	4855	S1M10000022F11	6097	S1M10000047E05		
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1131	E3M10000050E01	2373	E1M10000252B10	3615	P1M10000075C05	4857	S1M10000022A12	6099	S1M10000047G05		
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1133	E3M10000050B03	2375	E1M10000252E10	3617	P1M10000076D05	4859	S1M10000022G12	6101	S1M10000047A06		
1134	E3M10000050C03	2376	E1M10000252E11	3618	P1M10000076C08	4860	S1M10000023B01	6102	S1M10000047B06		
1135	E3M10000050D03	2377	E1M10000252E12	3619	P1M10000076D10	4861	S1M10000023D01	6103	S1M10000047C06		
1136	E3M10000050E03	2378	E1M10000253A02	3620	P1M10000077E04	4862	S1M10000023E01	6104	S1M10000047E06		
1137	E3M10000050A04	2379	E1M10000253G02	3621	P1M10000077H05	4863	S1M10000023G01	6105	S1M10000047F06		
1138	E3M10000050E04	2380	E1M10000253C04	3622	P1M10000077A08	4864	S1M10000023C02	6106	S1M10000047G06		
1139	E3M10000050H08	2381	E1M10000253D04	3623	P1M10000077C08	4865	S1M10000023G02	6107	S1M10000047A07		
1140	E3M10000052C01	2382	E1M10000253F04	3624	P1M10000096F01	4866	S1M10000023H02	6108	S1M10000047C07		
1141	E3M10000052F01	2383	E1M10000253H05	3625	P1M10000096E04	4867	S1M10000023B03	6109	S1M10000047D07		
1142	E3M10000052C02	2384	E1M10000253D08	3626	P1M10000096E12	4868	S1M10000023D03	6110	S1M10000047F07		
1143	E3M10000052D02	2385	E1M10000253E08	3627	P1M10000097G05	4869	S1M10000023G03	6111	S1M10000047G07		
1144	E3M10000052G02	2386	E1M10000253A09	3628	P1M10000059B04	4870	S1M10000023D04	6112	S1M10000047H07		
1145	E3M10000052B03	2387	E1M10000253D09	3629	P1M10000059H08	4871	S1M10000023E04	6113	S1M10000047A08		
1146	E3M10000052E03	2388	E1M10000253E09	3630	P1M10000059H09	4872	S1M10000023F04	6114	S1M10000047B08		
1147	E3M10000052G03	2389	E1M10000253F09	3631	P1M10000059B10	4873	S1M10000023A05	6115	S1M10000047C08		
1148	E3M10000052B04	2390	E1M10000253G09	3632	P1M10000059B11	4874	S1M10000023D05	6116	S1M10000047E08		
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1152	E3M10000052D05	2394	E1M10000253B11	3636	P1M10000060H04	4878	S1M10000023B07	6120	S1M10000047A09
1153	E3M10000052F05	2395	E1M10000253F11	3637	P1M10000079D01	4879	S1M10000023D07	6121	S1M10000047B09
1154	E3M10000052G05	2396	E1M10000253D12	3638	P1M10000079F06	4880	S1M10000023E07	6122	S1M10000047C09
1155	E3M10000052G06	2397	E1M10000253G12	3639	P1M10000079A10	4881	S1M10000023F07	6123	S1M10000047D09
1156	E3M10000052H06	2398	E1M10000254A03	3640	P1M10000079B10	4882	S1M10000023G07	6124	S1M10000047E09
1157	E3M10000052B07	2399	E1M10000254B03	3641	P1M10000079C10	4883	S1M10000023H07	6125	S1M10000047F09
1158	E3M10000052F08	2400	E1M10000254C03	3642	P1M10000079D10	4884	S1M10000023B08	6126	S1M10000047G09
1159	E3M10000052E09	2401	E1M10000254F03	3643	P1M10000080B01	4885	S1M10000023D08	6127	S1M10000047H09
1160	E3M10000052G09	2402	E1M10000254A04	3644	P1M10000080C01	4886	S1M10000023F08	6128	S1M10000047A10
1161	E3M10000052F10	2403	E1M10000254G05	3645	P1M10000080E04	4887	S1M10000023G08	6129	S1M10000047B10
1162	E3M10000052D11	2404	E1M10000254H05	3646	P1M10000080B06	4888	S1M10000023A09	6130	S1M10000047D10
1163	E3M10000052D12	2405	E1M10000254B06	3647	P1M10000080C06	4889	S1M10000023B09	6131	S1M10000047E10
1164	1008-H20	2406	E1M10000254A07	3648	P1M10000081G05	4890	S1M10000023D09	6132	S1M10000047F10
1165	1011-P20	2407	E1M10000254E07	3649	P1M10000081H05	4891	S1M10000023G09	6133	S1M10000047G10
1166	1053-37	2408	E1M10000254G07	3650	P1M10000081A06	4892	S1M10000023H09	6134	S1M10000047H10
1167	1010-C11	2409	E1M10000254A08	3651	P1M10000081D12	4893	S1M10000023B10	6135	S1M10000047A11
1168	1017-H1	2410	E1M10000254B09	3652	P1M10000082A02	4894	S1M10000023C10	6136	S1M10000047B11
1169	1067-16	2411	E1M10000254F10	3653	P1M10000082B04	4895	S1M10000023D10	6137	S1M10000047C11
1170	1083-27	2412	E1M10000254A11	3654	P1M10000082A05	4896	S1M10000023E10	6138	S1M10000047E11
1171	1065-12	2413	E1M10000254C11	3655	P1M10000082C05	4897	S1M10000023F10	6139	S1M10000047F11
1172	221-41	2414	E1M10000254E12	3656	P1M10000082D05	4898	S1M10000023H10	6140	S1M10000047H11
1173	B17-6.O10	2415	E1M10000255C01	3657	P1M10000082E05	4899	S1M10000023A11	6141	S1M10000047A12
1174	910-B20	2416	E1M10000255G02	3658	P1M10000083B01	4900	S1M10000023B11	6142	S1M10000047B12
1175	B18-2.N21	2417	E1M10000255H02	3659	P1M10000083A11	4901	S1M10000023C11	6143	S1M10000047C12
1176	971-B20	2418	E1M10000255A04	3660	P1M10000083B12	4902	S1M10000023E11	6144	S1M10000047D12
1177	D1-1.A15	2419	E1M10000255D05	3661	P1M10000083C12	4903	S1M10000023F11	6145	S1M10000047E12
1178	4-28.1	2420	E1M10000255F06	3662	P1M10000084D03	4904	S1M10000023G11	6146	S1M10000047F12
1179	D1-2.B13	2421	E1M10000255G06	3663	P1M10000084A04	4905	S1M10000023A12	6147	S1M10000048C01
1180	D1-2.F21	2422	E1M10000255B08	3664	P1M10000084E04	4906	S1M10000023B12	6148	S1M10000048D01
1181	Z56-D2	2423	E1M10000255D09	3665	P1M10000084F08	4907	S1M10000023C12	6149	S1M10000048G01
1182	PJMF55	2424	E1M10000255F09	3666	P1M10000084E11	4908	S1M10000023D12	6150	S1M10000048H01
1183	R1-15.A13	2425	E1M10000255B10	3667	P1M10000085D06	4909	S1M10000023F12	6151	S1M10000048A02
1184	R1-19.H1	2426	E1M10000256F01	3668	P1M10000086B01	4910	S1M10000024D01	6152	S1M10000048B02
1185	R1-55.M2	2427	E1M10000256B02	3669	P1M10000086E01	4911	S1M10000024A02	6153	S1M10000048C02

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1188	E1M10000007B04	2430	E1M10000256C05	3672	P1M10000086E05	4914	S1M10000024F02	6156	S1M10000048F02
1189	227-10	2431	E1M10000256E07	3673	P1M10000087E04	4915	S1M10000024H02	6157	S1M10000048G02
1190	709-F23	2432	E1M10000256E09	3674	P1M10000087F04	4916	S1M10000024D03	6158	S1M10000048H02
1191	801-C15	2433	E1M10000256A10	3675	P1M10000087C09	4917	S1M10000024E03	6159	S1M10000048A03
1192	801-H19	2434	E1M10000256F10	3676	P1M10000087F09	4918	S1M10000024F03	6160	S1M10000048B03
1193	804-P6	2435	E1M10000256C12	3677	P1M10000087A11	4919	S1M10000024A04	6161	S1M10000048C03
1194	807-D20	2436	E1M10000257C01	3678	P1M10000088C04	4920	S1M10000024C04	6162	S1M10000048E03
1195	B13-17.G8	2437	E1M10000257G01	3679	P1M10000088A07	4921	S1M10000024D04	6163	S1M10000048F03
1196	B5-6.C8	2438	E1M10000257A02	3680	P1M10000089G08	4922	S1M10000024H04	6164	S1M10000048G03
1197	B8-2.D9	2439	E1M10000257D02	3681	P1M10000089D11	4923	S1M10000024B05	6165	S1M10000048H03
1198	B15-8.P13	2440	E1M10000257H02	3682	P1M10000090E01	4924	S1M10000024E05	6166	S1M10000048E04
1199	T13-5.A2	2441	E1M10000257C03	3683	P1M10000090F06	4925	S1M10000024F05	6167	S1M10000048G04
1200	T12-3.I11	2442	E1M10000257F04	3684	P1M10000090F08	4926	S1M10000024G05	6168	S1M10000048H04
1201	T20-15.D4	2443	E1M10000257G04	3685	P1M10000090B11	4927	S1M10000024B06	6169	S1M10000048A05
1202	T24-15.G6	2444	E1M10000257B05	3686	P1M10000091A09	4928	S1M10000024E06	6170	S1M10000048B05
1203	T24-17.C6	2445	E1M10000257D05	3687	P1M10000091E09	4929	S1M10000024G06	6171	S1M10000048C05
1204	244.B12	2446	E1M10000257F06	3688	P1M10000091G10	4930	S1M10000024H06	6172	S1M10000048F05
1205	1042-J1	2447	E1M10000257G07	3689	P1M10000092B02	4931	S1M10000024A07	6173	S1M10000048G05
1206	195.F5	2448	E1M10000257H07	3690	P1M10000092E02	4932	S1M10000024C07	6174	S1M10000048H05
1207	25.D5	2449	E1M10000257H08	3691	P1M10000092B04	4933	S1M10000024E07	6175	S1M10000048A06
1208	25.D6	2450	E1M10000257A09	3692	P1M10000092F05	4934	S1M10000024G07	6176	S1M10000048B06
1209	177.F3	2451	E1M10000257D09	3693	P1M10000092F06	4935	S1M10000024H07	6177	S1M10000048C06
1210	525.H11	2452	E1M10000257G10	3694	P1M10000092D09	4936	S1M10000024A08	6178	S1M10000048E06
1211	632.N2	2453	E1M10000257H10	3695	P1M10000092B10	4937	S1M10000024B08	6179	S1M10000048A07
1212	633.B7	2454	E1M10000257A11	3696	P1M10000092B12	4938	S1M10000024E08	6180	S1M10000048C07
1213	671.I20	2455	E1M10000257C11	3697	P1M10000093A03	4939	S1M10000024F08	6181	S1M10000048E07
1214	676.B12	2456	E1M10000257F11	3698	P1M10000093B03	4940	S1M10000024G08	6182	S1M10000048F07
1215	643.B19	2457	E1M10000257B12	3699	P1M10000093F03	4941	S1M10000024H08	6183	S1M10000048G07
1216	720.O16	2458	E1M10000257F12	3700	P1M10000093H07	4942	S1M10000024B09	6184	S1M10000048H07
1217	666.H12	2459	E1M10000258C01	3701	P1M10000093C08	4943	S1M10000024B10	6185	S1M10000048B08
1218	98.D4	2460	E1M10000258H02	3702	P1M10000093B09	4944	S1M10000024D10	6186	S1M10000048C08
1219	844.B21	2461	E1M10000258G03	3703	P1M10000093E09	4945	S1M10000024F10	6187	S1M10000048D08
1220	P31-25-F3	2462	E1M10000258A04	3704	P1M10000094H03	4946	S1M10000024G10	6188	S1M10000048E08
1221	P335-8.H8	2463	E1M10000258C04	3705	P1M10000094F04	4947	S1M10000024A11	6189	S1M10000048F08

SeqID	Clone Name	SeqID	Clone Name	SeqID	Clone Name	SeqID	Clone Name	SeqID	Clone Name
1222	P347.2	2464	E1M10000258G04	3706	P1M10000094H04	4948	S1M10000024D11	6190	S1M10000048H08
1223	P31-11-J20	2465	E1M10000258C05	3707	P1M10000094A10	4949	S1M10000024G12	6191	S1M10000048A09
1224	P336-14.F20	2466	E1M10000258D05	3708	P1M10000095C01	4950	S1M10000025B01	6192	S1M10000048C09
1225	P31-27-M1	2467	E1M10000258F05	3709	P1M10000095E04	4951	S1M10000025C01	6193	S1M10000048D09
1226	P338-4.M21	2468	E1M10000258G05	3710	P1M10000095G04	4952	S1M10000025D01	6194	S1M10000048E09
1227	P334-8.L7	2469	E1M10000258A06	3711	P1M10000095C09	4953	S1M10000025E01	6195	S1M10000048F09
1228	P31-2-E16	2470	E1M10000258D06	3712	P1M10000102E05	4954	S1M10000025B02	6196	S1M10000048H09
1229	P335-3.J14	2471	E1M10000258B07	3713	P1M10000102B07	4955	S1M10000025A03	6197	S1M10000048A10
1230	P334-5.H2	2472	E1M10000258G07	3714	P1M10000103B05	4956	S1M10000025B03	6198	S1M10000048B10
1231	P31-33-N2	2473	E1M10000258G08	3715	P1M10000103D06	4957	S1M10000025C03	6199	S1M10000048C10
1232	P332-11.C20	2474	E1M10000258B09	3716	P1M10000103E08	4958	S1M10000025D03	6200	S1M10000048D10
1233	869.A23	2475	E1M10000258D09	3717	P1M10000104A02	4959	S1M10000025F03	6201	S1M10000048E10
1234	P317-2.A3	2476	E1M10000258F10	3718	P1M10000104H02	4960	S1M10000025D04	6202	S1M10000048G10
1235	P326-9.K2	2477	E1M10000258C11	3719	P1M10000104A03	4961	S1M10000025E04	6203	S1M10000048H10
1236	P323-8.P1	2478	E1M10000258F11	3720	P1M10000104E03	4962	S1M10000025G04	6204	S1M10000048A11
1237	P35-8	2479	E1M10000259C03	3721	P1M10000104F07	4963	S1M10000025B05	6205	S1M10000048C11
1238	P36-13.E2	2480	E1M10000259B04	3722	P1M10000104D11	4964	S1M10000025C05	6206	S1M10000048D11
1239	P38-1.G20	2481	E1M10000259E04	3723	P1M10000105D01	4965	S1M10000025F05	6207	S1M10000048F11
1240	P327-50.M10	2482	E1M10000259E05	3724	P1M10000105E02	4966	S1M10000025H05	6208	S1M10000048G11
1241	P328-8.D21	2483	E1M10000259B12	3725	P1M10000105C03	4967	S1M10000025B06	6209	S1M10000048H11
1242	P328-20.P20	2484	E1M10000260E02	3726	P1M10000105G03	4968	S1M10000025D06	6210	S1M10000048A12



## EXAMPLE 3

Comparison Of Isolated Nucleic Acids to Known Sequences

The nucleotide sequences of the subcloned fragments from *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Salmonella typhimurium* obtained from the expression vectors discussed above were compared to known sequences from *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium* and other microorganisms as follows. First, to confirm that each clone originated from one location on the chromosome and was not chimeric, the nucleotide sequences of the selected clones were compared against the *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* or *Salmonella typhimurium* genomic sequences to align the clone to the correct position on the chromosome. The NCBI BLASTN v 2.0.9 program was used for this comparison, and the incomplete *Staphylococcus aureus* genomic sequences licensed from TIGR, as well as the NCBI nonredundant GenBank database were used as the source of genomic data. *Salmonella typhimurium* sequences were compared to sequences available from the Genome Sequencing Center (<http://genome.wustl.edu/gsc/salmonella.shtml>), and the Sanger Centre ([http://www.sanger.ac.uk/projects/S\\_\\_typhi](http://www.sanger.ac.uk/projects/S__typhi)). *Pseudomonas aeruginosa* sequences were compared to a proprietary database and the NCBI GenBank database. The *E. faecalis* sequences were compared to a proprietary database.

The BLASTN analysis was performed using the default parameters except that the filtering was turned off. No further analysis was performed on inserts which resulted from the ligation of multiple fragments.

In general, antisense molecules and their complementary genes are identified as follows. First, all possible full length open reading frames (ORFs) are extracted from available genomic databases. Such databases include the GenBank nonredundant (nr) database, the unfinished genome database available from TIGR and the PathoSeq database developed by Incyte Genomics. The latter database comprises over 40 annotated bacterial genomes including complete ORF analysis. If databases are incomplete with regard to the bacterial genome of interest, it is not necessary to extract all ORFs in the genome but only to extract the ORFs within the portions of the available genomic sequences which are complementary to the clones of interest. Computer algorithms for identifying ORFs, such as GeneMark, are available and well known to those in the art. Comparison of the clone DNA to the complementary ORF(s) allows determination of whether the clone is a sense or antisense clone. Furthermore, each ORF extracted from the database can be compared to sequences in well annotated databases including the GenBank (nr) protein database, SWISSPROT and the like. A description of the gene or of a closely related gene in a closely related microorganism is often available in these databases. Similar methods are used to identify antisense clones corresponding to genes encoding non-translated RNAs.

In order to generate the gene identification data compiled in Table IB, each of the cloned nucleic acid sequences discussed above corresponding to SEQ ID NO.s 1-6213 was used to identify the corresponding *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* or *Salmonella typhimurium* ORFs in the PathoSeq v.4.1 (March 2000 release) database of microbial genomic sequences. For this purpose, the NCBI BLASTN 2.0.9 computer algorithm was used. The default parameters were used except that filtering was turned off. The default parameters for the BLASTN and BLASTX analyses were:

Expectation value (e)=10

Alignment view options: pairwise

10 Filter query sequence (DUST with BLASTN, SEG with others)=T

Cost to open a gap (zero invokes behavior)=0

Cost to extend a gap (zero invokes behavior)=0

X dropoff value for gapped alignment (in bits) (zero invokes behavior)=0

Show GI's in defines=F

15 Penalty for a nucleotide mismatch (BLASTN only)=!3

Reward for a nucleotide match (BLASTN only)=1

Number of one-line descriptions (V)=500

Number of alignments to show (B)=250

Threshold for extending hits=default

20 Perform gapped alignment (not available with BLASTX)=T

Query Genetic code to use=1

DB Genetic code (for TBLAST[nx] only)=1

Number of processors to use=1

SeqAlign file

25 Believe the query define=F

Matrix=BLOSUM62

Word Size= default

Effective length of the database (use zero for the real size)=0

Number of best hits from a region to keep=100

30 Length of region used to judge hits=20

Effective length of the search space (use zero for the real size)=0

Query strands to search against database (for BLAST[nx] and TBLASTX), 3 is both, 1 is top, 2 is bottom=3

Produce HTML output=F

35

Alternatively, ORFs were identified and refined by conducting a survey of the public and private data sources. Full-length gene protein and nucleotide sequences for these organisms were assembled from various sources. For *Pseudomonas aeruginosa*, gene sequences were adopted from the *Pseudomonas* genome sequencing project (downloaded from <http://www.pseudomonas.com>). For *Klebsiella pneumoniae*, *Staphylococcus aureus*, *Streptococcus pneumoniae* and *Salmonella typhi*, genomic sequences from PathoSeq v 4.1 (Mar 2000 release) was reanalyzed for ORFs using the gene finding software GeneMark v 2.4a, which was purchased from GenePro Inc. 451 Bishop St., N.W., Suite B, Atlanta, GA, 30318, USA.

45 Antisense clones were identified as those clones for which transcription from the inducible promoter would result in the expression of an RNA antisense to a complementary ORF, intergenic

or intragenic sequence. Those clones containing single inserts and that caused growth sensitivity upon induction are listed in Table IA.

The gene descriptions in the PathoSeq database derive from annotations available in the public sequence databases described above. Where a clone was found to share significant sequence  
5 identity to two or more adjacent ORFs, it was listed once for each ORF and the PathoSeq information for each ORF was compiled in Table IB.

Table IA lists the SEQ ID NOs. and clone names of the inserts which inhibited proliferation. This information was used to identify the ORFs (SEQ ID NOs.: 6214-42397) whose gene products (SEQ ID NOs. 42398-78581) were inhibited by the nucleic acids comprising the  
10 nucleotide sequences of SEQ ID NOs. 1-6213. Table IB lists the clone name and the PathoSeq Locus containing the clone.

TABLE IB

Clone Name	Gene LocusID	Clone Name	Gene LocusID	Clone Name	Gene LocusID
E3M10000001B01	EFA205257	E1M10000233C05	ECO103161	S1M10000005E05	SAU802496
E3M10000001B01	EFA205258	E1M10000233H05	ECO103224	S1M10000005C06	SAU802121
E3M10000001A02	EFA205257	E1M10000233H05	ECO103225	S1M10000005D06	SAU801183
E3M10000001A02	EFA205258	E1M10000233D08	ECO103185	S1M10000005D06	SAU801184
E3M10000001B02	EFA205225	E1M10000233F08	ECO103265	S1M10000005A07	SAU800967
E3M10000001B02	EFA201977	E1M10000233F08	ECO103266	S1M10000005B07	SAU802496
E3M10000001B02	EFA203137	E1M10000233A09	ECO104092	S1M10000005D07	SAU801264
E3M10000001C02	EFA200840	E1M10000233A09	ECO104093	S1M10000005A08	SAU802496
E3M10000001D02	EFA202003	E1M10000233E09	ECO103238	S1M10000005B08	SAU800548
E3M10000001E02	EFA200840	E1M10000233E09	ECO103239	S1M10000005D08	SAU800607
E3M10000001F02	EFA200807	E1M10000233F09	ECO103886	S1M10000005E08	SAU802496
E3M10000001G02	EFA205257	E1M10000233D10	ECO103242	S1M10000005B09	SAU800122
E3M10000001G02	EFA205258	E1M10000233D10	ECO103243	S1M10000005C09	SAU801481
E3M10000001H02	EFA200811	E1M10000233H10	ECO100094	S1M10000005D09	SAU800542
E3M10000001E03	EFA201987	E1M10000234E01	ECO103884	S1M10000005A10	SAU801723
E3M10000001E03	EFA205258	E1M10000234B02	ECO103886	S1M10000005A10	SAU801722
E3M10000001G03	EFA201987	E1M10000234G02	ECO103233	S1M10000005A11	SAU801644
E3M10000001G03	EFA205258	E1M10000234G02	ECO103234	S1M10000005C11	SAU801113
E3M10000001H03	EFA201987	E1M10000234C05	ECO103181	S1M10000005D11	SAU800547
E3M10000001H03	EFA205258	E1M10000234C07	ECO103844	S1M10000005E11	SAU800155
E3M10000001D04	EFA201980	E1M10000234C08	ECO103878	S1M10000005B12	SAU802160
E3M10000001D04	EFA201981	E1M10000234C08	ECO204942	S1M10000005B12	SAU603460
E3M10000001D04	EFA205229	E1M10000234F08	ECO103461	S1M10000005D12	SAU801644
E3M10000001E04	EFA201028	E1M10000234H08	ECO103226	S1M10000006F01	SAU801264
E3M10000001F04	EFA200811	E1M10000234F09	ECO103055	S1M10000006B02	SAU800381
E3M10000001G04	EFA201993	E1M10000234D10	ECO100876	S1M10000006E02	SAU802496
E3M10000001H04	EFA201980	E1M10000234G10	ECO100886	S1M10000006F02	SAU802160
E3M10000001H04	EFA201981	E1M10000234B12	ECO104010	S1M10000006G02	SAU802125
E3M10000001H04	EFA205229	E1M10000235D01	ECO102233	S1M10000006A03	SAU802496
E3M10000001B05	EFA201993	E1M10000235A03	ECO100798	S1M10000006B03	SAU802655
E3M10000001D05	EFA201974	E1M10000235H03	ECO103886	S1M10000006D03	SAU801740
E3M10000001D05	EFA201975	E1M10000235E04	ECO103236	S1M10000006E03	SAU801256
E3M10000001G05	EFA202001	E1M10000235B06	ECO103886	S1M10000006F03	SAU801434
E3M10000001G05	EFA202003	E1M10000235F06	ECO103481	S1M10000006G03	SAU801275
E3M10000001A06	EFA201028	E1M10000235B08	ECO103885	S1M10000006A04	SAU801139
E3M10000001F06	EFA201028	E1M10000235E08	ECO103161	S1M10000006B04	SAU802496
E3M10000001B08	EFA201028	E1M10000235B09	ECO101848	S1M10000006C04	SAU802158
E3M10000001E08	EFA200807	E1M10000235H09	ECO103481	S1M10000006E04	SAU801089
E3M10000001C09	EFA200839	E1M10000235H09	ECO103482	S1M10000006F04	SAU801644
E3M10000001D09	EFA201987	E1M10000235B10	ECO100886	S1M10000006G04	SAU801740
E3M10000001D09	EFA205258	E1M10000235A11	ECO102299	S1M10000006A05	SAU802224
E3M10000001E09	EFA201987	E1M10000235F12	ECO103233	S1M10000006A05	SAU802223
E3M10000001E09	EFA205258	E1M10000235F12	ECO103234	S1M10000006D05	SAU802496
E3M10000001B10	EFA205257	E1M10000236E01	ECO100095	S1M10000006G05	SAU801256
E3M10000001B10	EFA205258	E1M10000236A02	ECO102340	S1M10000006C06	SAU800331
E3M10000004D01	EFA201985	E1M10000236E02	ECO103878	S1M10000006C06	SAU800332
E3M10000004D01	EFA201984	E1M10000236E02	ECO204942	S1M10000006D06	SAU802496
E3M10000004D01	EFA202953	E1M10000236A03	ECO103287	S1M10000006F06	SAU800548
E3M10000004G01	EFA200839	E1M10000236D03	ECO102556	S1M10000006G06	SAU800006
E3M10000004D02	EFA202022	E1M10000236G03	ECO102655	S1M10000006A07	SAU800967
E3M10000004D02	EFA202028	E1M10000236A04	ECO103186	S1M10000006B07	SAU801760

Clone Name	Gene LocusID	Clone Name	Gene LocusID	Clone Name	Gene LocusID
E3M10000004D02	EFA202536	E1M10000236D04	ECO103481	S1M10000006C07	SAU800546
E3M10000004C03	EFA200412	E1M10000236G04	ECO103510	S1M10000006D07	SAU801105
E3M10000004A04	EFA201981	E1M10000236A05	ECO102847	S1M10000006E07	SAU802496
E3M10000004A04	EFA205229	E1M10000236F05	ECO103181	S1M10000006G07	SAU801731
E3M10000004F08	EFA201977	E1M10000236F05	ECO103182	S1M10000006A08	SAU802496
E3M10000004F08	EFA203137	E1M10000236H06	ECO103242	S1M10000006E08	SAU802238
E3M10000004D10	EFA201999	E1M10000236H06	ECO103243	S1M10000006A10	SAU802496
E3M10000004D10	EFA201997	E1M10000236D08	ECO103669	S1M10000006B10	SAU802240
E3M10000004F10	EFA200624	E1M10000236F09	ECO103228	S1M10000006C10	SAU802496
E3M10000004E11	EFA200624	E1M10000236C10	ECO102227	S1M10000006G10	SAU802247
E3M10000004H11	EFA205225	E1M10000236A11	ECO102986	S1M10000006G10	SAU802248
E3M10000004H11	EFA201977	E1M10000236C11	ECO101088	S1M10000006B11	SAU801618
E3M10000004H11	EFA203137	E1M10000236F12	ECO101355	S1M10000006G11	SAU802119
E3M10000005B01	EFA201984	E1M10000237A02	ECO103161	S1M10000006G11	SAU802118
E3M10000005B01	EFA201983	E1M10000237B02	ECO101830	S1M10000006A12	SAU800548
E3M10000005C01	EFA200839	E1M10000237E04	ECO103217	S1M10000006B12	SAU802558
E3M10000005E01	EFA201977	E1M10000237E04	ECO103218	S1M10000007F01	SAU801256
E3M10000005E01	EFA203137	E1M10000237H04	ECO103624	S1M10000007B02	SAU800591
E3M10000005E02	EFA201977	E1M10000237H04	ECO103625	S1M10000007B02	SAU800592
E3M10000005E02	EFA203137	E1M10000237G06	ECO103232	S1M10000007F02	SAU801366
E3M10000005C03	EFA200811	E1M10000237G06	ECO103233	S1M10000007G02	SAU801138
E3M10000005C03	EFA200812	E1M10000237C07	ECO103886	S1M10000007A03	SAU801899
E3M10000005D03	EFA200811	E1M10000237G07	ECO103263	S1M10000007D03	SAU802496
E3M10000005D03	EFA200812	E1M10000237H07	ECO102267	S1M10000007G03	SAU800967
E3M10000005E03	EFA200811	E1M10000237A08	ECO103217	S1M10000007C04	SAU801740
E3M10000005E03	EFA200812	E1M10000237A08	ECO103216	S1M10000007E04	SAU802496
E3M10000005C04	EFA200660	E1M10000237B08	ECO101185	S1M10000007F04	SAU800478
E3M10000005C04	EFA200661	E1M10000237B08	ECO101186	S1M10000007C05	SAU800547
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E3M10000005G05	EFA203137	E1M10000237E08	ECO103878	S1M10000007E06	SAU801113
E3M10000005A07	EFA200811	E1M10000237E08	ECO204942	S1M10000007C07	SAU801904
E3M10000005A07	EFA200812	E1M10000237B09	ECO101844	S1M10000007E07	SAU801618
E3M10000005F07	EFA200839	E1M10000237D10	ECO102060	S1M10000007G07	SAU802638
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E3M10000005B08	EFA203137	E1M10000237E11	ECO100169	S1M10000007E08	SAU800700
E3M10000005E08	EFA202276	E1M10000238G01	ECO103451	S1M10000007F08	SAU802261
E3M10000005D10	EFA201977	E1M10000238A02	ECO103514	S1M10000007F09	SAU800210
E3M10000005D10	EFA203137	E1M10000238F03	ECO101939	S1M10000007D10	SAU800537
E3M10000005F10	EFA201977	E1M10000238B04	ECO103262	S1M10000007F10	SAU802240
E3M10000005F10	EFA203137	E1M10000238B04	ECO103878	S1M10000007B11	SAU802177
E3M10000006C01	EFA201982	E1M10000238B04	ECO204942	S1M10000007B11	SAU802176
E3M10000006C01	EFA201981	E1M10000238D04	ECO104147	S1M10000007D11	SAU801900
E3M10000006G02	EFA202214	E1M10000238F04	ECO103224	S1M10000008F01	SAU802160
E3M10000006G02	EFA202216	E1M10000238F04	ECO103225	S1M10000008F01	SAU603460
E3M10000006B03	EFA201999	E1M10000238E05	ECO103263	S1M10000008F02	SAU800519
E3M10000006B03	EFA201997	E1M10000238F05	ECO100194	S1M10000008G02	SAU802643
E3M10000006D03	EFA201982	E1M10000238F05	ECO100195	S1M10000008A03	SAU802177
E3M10000006D03	EFA201981	E1M10000238D06	ECO101185	S1M10000008A03	SAU802176
E3M10000006F04	EFA200811	E1M10000238D06	ECO101186	S1M10000008B03	SAU800023
E3M10000006F04	EFA200812	E1M10000238F06	ECO103229	S1M10000008F03	SAU800753
E3M10000006G04	EFA201999	E1M10000238F06	ECO103230	S1M10000008G03	SAU802369

Clone Name	Gene LocusID	Clone Name	Gene LocusID	Clone Name	Gene LocusID
E3M10000006G04	EFA201997	E1M10000238A07	ECO103236	S1M10000008A04	SAU800478
E3M10000006H09	EFA201028	E1M10000238A07	ECO103237	S1M10000008B04	SAU802496
E3M10000006E11	EFA200811	E1M10000238A08	ECO101628	S1M10000008D05	SAU800517
E3M10000006E11	EFA200812	E1M10000238E08	ECO103237	S1M10000008D05	SAU202623
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E3M10000051F07	EFA201970	E1M10000289E07	ECO100095	S1M10000028B09	SAU800547
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E3M10000050G01	EFA200179	E1M10000290E08	ECO102555	S1M10000029G05	SAU801253
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E3M10000052G02	EFA200457	E1M10000291B04	ECO103238	S1M10000029C10	SAU800529
E3M10000052B03	EFA200239	E1M10000291E04	ECO100967	S1M10000029D10	SAU801790
E3M10000052E03	EFA202378	E1M10000291E05	ECO103223	S1M10000029E10	SAU801139
E3M10000052G03	EFA200326	E1M10000291G05	ECO102555	S1M10000029F10	SAU800266
E3M10000052B04	EFA200290	E1M10000291G05	ECO102556	S1M10000029H10	SAU801139

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E3M10000052D05	EFA201888	E1M10000291E07	ECO103866	S1M10000029C12	SAU802070
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E3M10000052G06	EFA202274	E1M10000291B08	ECO103218	S1M10000029F12	SAU800257
E3M10000052H06	EFA200805	E1M10000291F08	ECO103229	S1M10000029G12	SAU801138
E3M10000052B07	EFA202168	E1M10000291B10	ECO103881	S1M10000030B01	SAU802654
E3M10000052F08	EFA202378	E1M10000291E10	ECO101591	S1M10000030D01	SAU801113
E3M10000052E09	EFA201985	E1M10000291D11	ECO103263	S1M10000030F01	SAU801473
E3M10000052E09	EFA202953	E1M10000291F11	ECO100095	S1M10000030H01	SAU800543
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E3M10000052F10	EFA200240	E1M10000291H11	ECO103262	S1M10000030C02	SAU802567
E3M10000052D11	EFA200898	E1M10000291H11	ECO103878	S1M10000030D02	SAU801515
E3M10000052D12	EFA202168	E1M10000291H11	ECO204942	S1M10000030E02	SAU801473
1008-H20	ECO100023	E1M10000291B12	ECO103882	S1M10000030H02	SAU802452
1011-P20	ECO100702	E1M10000291F12	ECO103243	S1M10000030B03	SAU802654
1053-37	ECO101256	E1M10000293B01	ECO103885	S1M10000030C03	SAU800275
1053-37	ECO202228	E1M10000293B02	ECO104093	S1M10000030D03	SAU801473
1010-C11	ECO101324	E1M10000293G02	ECO103886	S1M10000030G03	SAU800542
1017-H1	ECO304472	E1M10000293A04	ECO100402	S1M10000030H03	SAU800232
1067-16	ECO102309	E1M10000293B04	ECO103886	S1M10000030C04	SAU800526
1083-27	ECO102636	E1M10000293A05	ECO100095	S1M10000030A05	SAU800478
1065-12	ECO102557	E1M10000293E05	ECO103223	S1M10000030B05	SAU801256
221-41	ECO103884	E1M10000293E05	ECO103224	S1M10000030C05	SAU800526
B17-6.O10	ECO103884	E1M10000293G05	ECO103243	S1M10000030D05	SAU800759
910-B20	ECO103884	E1M10000293A06	ECO101175	S1M10000030D05	SAU302793
B18-2.N21	ECO100148	E1M10000293H06	ECO102654	S1M10000030G05	SAU800776
971-B20	ECO103240	E1M10000293F07	ECO101095	S1M10000030G05	SAU800777
971-B20	ECO103241	E1M10000293C08	ECO101844	S1M10000030H05	SAU800179
D1-1.A15	ECO103394	E1M10000293E08	ECO101939	S1M10000030D06	SAU800189
4-28.1	ECO101485	E1M10000293G08	ECO103101	S1M10000030E06	SAU801257
D1-2.B13	ECO102255	E1M10000293B09	ECO103181	S1M10000030B07	SAU802627
D1-2.P21	ECO102144	E1M10000293G09	ECO102144	S1M10000030D07	SAU800189
Z56-D2	ECO103911	E1M10000293H09	ECO100094	S1M10000030G07	SAU802247
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R1-15.A13	ECO101995	E1M10000293E11	ECO103242	S1M10000030F08	SAU802231
R1-19.H1	ECO101104	E1M10000293F11	ECO104091	S1M10000030F08	SAU802230
R1-55.M2	ECO103884	E1M10000293F11	ECO104092	S1M10000030G08	SAU802250
Z45-F11	ECO103263	E1M10000293C12	ECO100170	S1M10000030A09	SAU801719
Z8-B9	ECO102033	E1M10000293D12	ECO103221	S1M10000030B09	SAU802654
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709-F23	ECO101506	E1M10000295G01	ECO103532	S1M10000030F09	SAU801904
801-C15	ECO100488	E1M10000295G01	ECO103533	S1M10000030G09	SAU800542
801-C15	ECO100490	E1M10000295B02	ECO101635	S1M10000030H09	SAU801644
801-C15	ECO100491	E1M10000295E02	ECO103217	S1M10000030A10	SAU802309
801-H19	ECO100488	E1M10000295E02	ECO103218	S1M10000030A10	SAU802308
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807-D20	ECO100366	E1M10000295B07	ECO100179	S1M10000030G10	SAU800019
807-D20	ECO100367	E1M10000295B07	ECO100180	S1M10000030H10	SAU802654
B13-17.G8	ECO101111	E1M10000295C07	ECO103224	S1M10000030A11	SAU800517
B5-6.C8	ECO101475	E1M10000295C07	ECO103225	S1M10000030A11	SAU202623
B5-6.C8	ECO101476	E1M10000295C07	ECO103226	S1M10000030D11	SAU800517
B5-6.C8	ECO201962	E1M10000295D08	ECO103225	S1M10000030D11	SAU202623
B8-2.D9	ECO103461	E1M10000295D08	ECO103226	S1M10000030E11	SAU802241
B15-8.P13	ECO101328	E1M10000295F08	ECO103160	S1M10000030G11	SAU800811
B15-8.P13	ECO101329	E1M10000295G08	ECO103217	S1M10000030C12	SAU801647
T13-5.A2	ECO103059	E1M10000295G08	ECO103218	S1M10000030C12	SAU801646
T12-3.I11	ECO102857	E1M10000295B09	ECO103236	S1M10000030E12	SAU800537
T20-15.D4	ECO101475	E1M10000295F09	ECO103881	S1M10000030G12	SAU801526
T20-15.D4	ECO101476	E1M10000295F09	ECO103882	S1M10000031B01	SAU802240
T20-15.D4	ECO201962	E1M10000295G09	ECO103263	S1M10000031H01	SAU800023
T24-15.G6	ECO103059	E1M10000295D10	ECO103101	S1M10000031B02	SAU802247
T24-17.C6	ECO102857	E1M10000295H10	ECO103263	S1M10000031E02	SAU801912
244.B12	ECO101763	E1M10000295B11	ECO103229	S1M10000031F02	SAU802231
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244.B12	ECO101765	E1M10000295G12	ECO103494	S1M10000031G02	SAU802235
1042-J1	ECO100702	E1M10000312D11	ECO104091	S1M10000031G02	SAU802234
1042-J1	ECO100703	E1M10000312D11	ECO104092	S1M10000031H02	SAU801355
195.F5	ECO102842	E1M10000296B01	ECO102304	S1M10000031A03	SAU802250
25.D5	ECO103059	E1M10000296C02	ECO102466	S1M10000031E03	SAU801134
25.D6	ECO103059	E1M10000296C02	ECO102467	S1M10000031E03	SAU801135
177.F3	ECO102309	E1M10000296D02	ECO103235	S1M10000031F03	SAU802240
525.H11	ECO102857	E1M10000296D02	ECO103236	S1M10000031G03	SAU801505
632.N2	ECO104277	E1M10000296D02	ECO103237	S1M10000031A04	SAU801434
633.B7	ECO103479	E1M10000296H02	ECO102556	S1M10000031A04	SAU302892
671.I20	ECO103478	E1M10000296C03	ECO100150	S1M10000031B04	SAU800543
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643.B19	ECO100702	E1M10000296E03	ECO101086	S1M10000031C04	SAU800737
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666.H12	ECO103478	E1M10000296H03	ECO103228	S1M10000031F04	SAU801517
666.H12	ECO103479	E1M10000296D04	ECO103237	S1M10000031F04	SAU801516
98.D4	ECO103263	E1M10000296G04	ECO102144	S1M10000031G04	SAU302611
844.B21	ECO102144	E1M10000296F05	ECO103886	S1M10000031G04	SAU302882
P31-25-F3	ECO101686	E1M10000296G05	ECO101467	S1M10000031F05	SAU800548
P335-8.H8	ECO101041	E1M10000296H05	ECO103094	S1M10000031D06	SAU801526
P347.2	ECO101086	E1M10000296A06	ECO100194	S1M10000031G06	SAU800548
P31-11-J20	ECO103228	E1M10000296A06	ECO100195	S1M10000031H06	SAU600582
P336-14.F20	ECO101370	E1M10000296G07	ECO102827	S1M10000031C07	SAU801760
P31-27-M1	ECO103423	E1M10000296G07	ECO102828	S1M10000031D07	SAU801181
P338-4.M21	ECO100139	E1M10000296H07	ECO103220	S1M10000031E07	SAU800016
P334-8.L7	ECO101256	E1M10000296H07	ECO103221	S1M10000031A08	SAU802365
P31-2-E16	ECO101686	E1M10000296E08	ECO100886	S1M10000031D08	SAU801790
P335-3.J14	ECO100523	E1M10000296F08	ECO103218	S1M10000031E08	SAU800547
P334-5.H2	ECO100139	E1M10000296G08	ECO103734	S1M10000031F08	SAU801264
P31-33-N2	ECO103241	E1M10000296H08	ECO100809	S1M10000031C09	SAU801193
P332-11.C20	ECO102827	E1M10000296H08	ECO100810	S1M10000031D09	SAU800019
P332-11.C20	ECO102828	E1M10000296A09	ECO100194	S1M10000031G09	SAU800006
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P326-9.K2	ECO103293	E1M10000296F12	ECO101684	S1M10000031E10	SAU800001
P323-8.P1	ECO101685	E1M10000296G12	ECO100095	S1M10000031F10	SAU800244
P35-8	ECO103692	E1M10000298C01	ECO101438	S1M10000031G10	SAU800962
P36-13.E2	ECO103059	E1M10000298G01	ECO104148	S1M10000031A11	SAU801741
P38-1.G20	ECO102227	E1M10000298G01	ECO104149	S1M10000031B11	SAU801908
P327-50.M10	ECO103242	E1M10000298G02	ECO102636	S1M10000031C11	SAU802152
P327-50.M10	ECO103243	E1M10000298C03	ECO103238	S1M10000031F11	SAU800312
P328-8.D21	ECO103240	E1M10000298C03	ECO103239	S1M10000031G11	SAU801234
P328-8.D21	ECO103241	E1M10000298D03	ECO103886	S1M10000031H11	SAU800962
P328-20.P20	ECO100541	E1M10000298H03	ECO103262	S1M10000031B12	SAU801621
P33-1.C22	ECO103227	E1M10000298H03	ECO103878	S1M10000031C12	SAU801741
X3S107-17	ECO101475	E1M10000298H03	ECO204942	S1M10000031E12	SAU801275
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X3S107-17	ECO201962	E1M10000298E04	ECO100431	S1M10000032B01	SAU802654
P35-7	ECO103928	E1M10000298H04	ECO100809	S1M10000032C01	SAU800548
X3S118-9	ECO103263	E1M10000298H04	ECO100808	S1M10000032F01	SAU800525
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X3S177-4	ECO101161	E1M10000298C05	ECO103236	S1M10000032H01	SAU802111
P342-3	ECO102104	E1M10000298D05	ECO101539	S1M10000032E02	SAU801096
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SC13.1	ECO101348	E1M10000298G06	ECO100096	S1M10000032C03	SAU800771
MC9.6	ECO102929	E1M10000298B07	ECO100095	S1M10000032D03	SAU801235
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E1M10000189A04	ECO103624	P1M10000038B08	PAE204067	S1M10000038D02	SAU801392
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E1M10000220E05	ECO101257	S1M10000002E09	SAU800547	S1M10000047E06	SAU802224
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E1M10000225B06	ECO101259	S1M10000003F12	SAU801621	S1M10000048G01	SAU800363
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E1M10000226B02	ECO103515	S1M10000004A04	SAU802655	S1M10000048B03	SAU801184
E1M10000226B02	ECO204900	S1M10000004B04	SAU801760	S1M10000048C03	SAU802586
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E1M10000226F02	ECO102999	S1M10000004D04	SAU802223	S1M10000048E03	SAU802586
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E1M10000226A08	ECO104132	S1M10000004E06	SAU802240	S1M10000048G04	SAU802247
E1M10000226D08	ECO101753	S1M10000004F06	SAU800152	S1M10000048H04	SAU802586
E1M10000226D09	ECO100430	S1M10000004A07	SAU802503	S1M10000048H04	SAU802585
E1M10000226D09	ECO100431	S1M10000004D07	SAU802496	S1M10000048A05	SAU801263
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E1M10000226D10	ECO101623	S1M10000004E07	SAU802176	S1M10000048C05	SAU801891
E1M10000226E10	ECO102714	S1M10000004F07	SAU801683	S1M10000048F05	SAU801184
E1M10000226G11	ECO103244	S1M10000004G07	SAU801644	S1M10000048G05	SAU800542
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E1M10000226F12	ECO100240	S1M10000004B08	SAU801346	S1M10000048A06	SAU800546
E1M10000227E03	ECO100975	S1M10000004B08	SAU200535	S1M10000048B06	SAU801184
E1M10000227E03	ECO201249	S1M10000004C08	SAU802503	S1M10000048C06	SAU801670
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E1M10000227C05	ECO104165	S1M10000004C09	SAU802496	S1M10000048G07	SAU800520
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E1M10000227B09	ECO102736	S1M10000004A11	SAU801475	S1M10000048E08	SAU802224
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E1M10000227D12	ECO104144	S1M10000004E12	SAU800528	S1M10000048F09	SAU802238
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E1M10000232B03	ECO101324	S1M10000005C01	SAU802496	S1M10000048C10	SAU800367
E1M10000232H03	ECO103097	S1M10000005E01	SAU800996	S1M10000048D10	SAU802590
E1M10000232C07	ECO100170	S1M10000005B02	SAU802243	S1M10000048E10	SAU802590
E1M10000232F07	ECO103797	S1M10000005D02	SAU800519	S1M10000048G10	SAU802238
E1M10000232F07	ECO103798	S1M10000005E02	SAU802655	S1M10000048H10	SAU802240
E1M10000232G07	ECO104010	S1M10000005F02	SAU801644	S1M10000048A11	SAU802224
E1M10000232A08	ECO100850	S1M10000005F02	SAU801643	S1M10000048C11	SAU802217
E1M10000232G08	ECO100875	S1M10000005A03	SAU802310	S1M10000048D11	SAU802090
E1M10000232G12	ECO102636	S1M10000005D03	SAU800548	S1M10000048F11	SAU802496
E1M10000233C01	ECO103886	S1M10000005F03	SAU802262	S1M10000048G11	SAU801186
E1M10000233A03	ECO100784	S1M10000005B04	SAU801183	S1M10000048H11	SAU801139
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E1M10000233D03	ECO100118	S1M10000005D04	SAU801184	S1M10000048B12	SAU802502
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E1M10000233H03	ECO103239	S1M10000005F04	SAU800362	S1M10000048D12	SAU800249
E1M10000233C04	ECO102309	S1M10000005F04	SAU800361	S1M10000048G12	SAU802251
E1M10000233G04	ECO101185	S1M10000005C05	SAU801264		
E1M10000233A05	ECO102553	S1M10000005D05	SAU801644		

Table IC provides a cross reference between PathoSeq Gene Loci listed in Table IB and the SEQ ID NOs. of the corresponding PathoSeq polypeptides and the SEQ ID NOs. of the nucleic acids which encode them. The Gene Locus IDs provided in Table IC each comprise a nine digit alpha-numeric identifier that can be used to determine the organism from which each Gene Locus and corresponding SEQ ID NOs. were identified. Specifically, the first letter of the Gene Locus ID corresponds to the first letter of the genus name of the organism described herein from which the Gene Locus was identified and the second and third letters of the Gene Locus ID correspond to the first two letters of the species name of this organism. For example, the identifier EFA205257 describes a gene locus identified from *Enterococcus faecalis*. In those instances where the three letter identifier is the same for different organisms, the exact identity of the organism which corresponds to the Gene Locus ID can be determined by referring to the organism designation in the sequence listing for the coding nucleic acid or polypeptide SEQ ID NO. that corresponds to the particular Gene Locus ID.

TABLE IC

DNA SeqID	Protein SeqID	Gene LocusID	DNA SeqID	Protein SeqID	Gene LocusID	DNA SeqID	Protein SeqID	Gene LocusID
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6216	42400	EFA205225	18278	54462	CJU100855	30339	66523	PAE203656
6217	42401	EFA201977	18279	54463	CJU100856	30340	66524	PAE203658
6218	42402	EFA203137	18280	54464	CJU100859	30341	66525	PAE203668
6219	42403	EFA200840	18281	54465	CJU100860	30342	66526	PAE203670
6220	42404	EFA202003	18282	54466	CJU100861	30343	66527	PAE203672
6221	42405	EFA200807	18283	54467	CJU100862	30344	66528	PAE203677
6222	42406	EFA200811	18284	54468	CJU100863	30345	66529	PAE203684
6223	42407	EFA201987	18285	54469	CJU100866	30346	66530	PAE203691
6224	42408	EFA201980	18286	54470	CJU100870	30347	66531	PAE203698
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6226	42410	EFA205229	18288	54472	CJU100872	30349	66533	PAE203732
6227	42411	EFA201028	18289	54473	CJU100885	30350	66534	PAE203735
6228	42412	EFA201993	18290	54474	CJU100886	30351	66535	PAE203739
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6230	42414	EFA201975	18292	54476	CJU100890	30353	66537	PAE203741
6231	42415	EFA202001	18293	54477	CJU100891	30354	66538	PAE203742
6232	42416	EFA200839	18294	54478	CJU100896	30355	66539	PAE203743
6233	42417	EFA201985	18295	54479	CJU100903	30356	66540	PAE203744
6234	42418	EFA201984	18296	54480	CJU100923	30357	66541	PAE203751
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6238	42422	EFA202536	18300	54484	CJU100944	30361	66545	PAE203758
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6246	42430	EFA200661	18308	54492	CJU100980	30369	66553	PAE203801
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6250	42434	EFA202216	18312	54496	CJU100989	30373	66557	PAE203820
6251	42435	EFA200360	18313	54497	CJU100993	30374	66558	PAE203821
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6254	42438	EFA201637	18316	54500	CJU100998	30377	66561	PAE203831
6255	42439	EFA201986	18317	54501	CJU100999	30378	66562	PAE203850
6256	42440	EFA205255	18318	54502	CJU101006	30379	66563	PAE203869
6257	42441	EFA200495	18319	54503	CJU101007	30380	66564	PAE203871
6258	42442	EFA104836	18320	54504	CJU101011	30381	66565	PAE203872
6259	42443	EFA201976	18321	54505	CJU101017	30382	66566	PAE203887
6260	42444	EFA201523	18322	54506	CJU101021	30383	66567	PAE203888
6261	42445	EFA202012	18323	54507	CJU101022	30384	66568	PAE203892
6262	42446	EFA202007	18324	54508	CJU101027	30385	66569	PAE203897
6263	42447	EFA200307	18325	54509	CJU101028	30386	66570	PAE203898
6264	42448	EFA201888	18326	54510	CJU101029	30387	66571	PAE203900
6265	42449	EFA205285	18327	54511	CJU101031	30388	66572	PAE203911

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6268	42452	EFA201611	18330	54514	CJU101046	30391	66575	PAE203920			
6269	42453	EFA201946	18331	54515	CJU101050	30392	66576	PAE203943			
6270	42454	EFA201512	18332	54516	CJU101054	30393	66577	PAE203958			
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6439	42623	ECO101111	18501	54685	CPN200011	30562	66746	PAE204887
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6442	42626	ECO201962	18504	54688	CPN200015	30565	66749	PAE204914
6443	42627	ECO103461	18505	54689	CPN200024	30566	66750	PAE204915
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6482	42666	ECO102087	18544	54728	CPN200112	30605	66789	PAE205119
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6484	42668	ECO101348	18546	54730	CPN200114	30607	66791	PAE205124
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7174	43358	ECO100808	19236	55420	EBC100486	31297	67481	PPU100113			
7175	43359	ECO101539	19237	55421	EBC100487	31298	67482	PPU100120			
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7187	43371	ECO204448	19249	55433	EBC100597	31310	67494	PPU100260			
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7190	43374	ECO104241	19252	55436	EBC100624	31313	67497	PPU100404			
7191	43375	ECO102363	19253	55437	EBC100628	31314	67498	PPU100405			
7192	43376	ECO100980	19254	55438	EBC100631	31315	67499	PPU100406			
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7194	43378	ECO103454	19256	55440	EBC100646	31317	67501	PPU100429			
7195	43379	ECO204438	19257	55441	EBC100653	31318	67502	PPU100453			
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7197	43381	ECO102066	19259	55443	EBC100655	31320	67504	PPU100484			
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7207	43391	ECO104233	19269	55453	EBC100703	31330	67514	PPU100635
7208	43392	ECO101499	19270	55454	EBC100704	31331	67515	PPU100641
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7214	43398	KPN103883	19276	55460	EBC100767	31337	67521	PPU100810
7215	43399	KPN208757	19277	55461	EBC100769	31338	67522	PPU100841
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7230	43414	KPN203534	19292	55476	EBC100833	31353	67537	PPU101006
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7239	43423	PAE201546	19301	55485	EBC100878	31362	67546	PPU101069
7240	43424	PAE202422	19302	55486	EBC100895	31363	67547	PPU101071
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7243	43427	PAE203039	19305	55489	EBC100906	31366	67550	PPU101093
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7245	43429	PAE204262	19307	55491	EBC100918	31368	67552	PPU101118
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7248	43432	PAE204270	19310	55494	EBC100928	31371	67555	PPU101137
7249	43433	PAE203045	19311	55495	EBC100940	31372	67556	PPU101138
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7253	43437	PAE202311	19315	55499	EBC100964	31376	67560	PPU101155
7254	43438	PAE203158	19316	55500	EBC100965	31377	67561	PPU101164
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7259	43443	PAE203011	19321	55505	EBC100985	31382	67566	PPU101175
7260	43444	PAE202220	19322	55506	EBC100989	31383	67567	PPU101184
7261	43445	PAE200714	19323	55507	EBC101014	31384	67568	PPU101189
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7264	43448	PAE203009	19326	55510	EBC101030	31387	67571	PPU101233
7265	43449	PAE204255	19327	55511	EBC101032	31388	67572	PPU101236
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7269	43453	PAE201300	19331	55515	EBC101043	31392	67576	PPU101392
7270	43454	PAE200352	19332	55516	EBC101051	31393	67577	PPU101395
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7274	43458	PAE203981	19336	55520	EBC101089	31397	67581	PPU101429
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7276	43460	PAE203003	19338	55522	EBC101094	31399	67583	PPU101447
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7278	43462	PAE204243	19340	55524	EBC101110	31401	67585	PPU101463
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7308	43492	PAE204504	19370	55554	EBC101242	31431	67615	PPU101821
7309	43493	PAE204256	19371	55555	EBC101244	31432	67616	PPU101826
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7314	43498	PAE200937	19376	55560	EBC101260	31437	67621	PPU101855
7315	43499	PAE201397	19377	55561	EBC101263	31438	67622	PPU101878
7316	43500	PAE201269	19378	55562	EBC101268	31439	67623	PPU101891
7317	43501	PAE205431	19379	55563	EBC101277	31440	67624	PPU101916
7318	43502	PAE205502	19380	55564	EBC101279	31441	67625	PPU101949
7319	43503	PAE201492	19381	55565	EBC101280	31442	67626	PPU101950
7320	43504	PAE203475	19382	55566	EBC101281	31443	67627	PPU101952
7321	43505	PAE202632	19383	55567	EBC101282	31444	67628	PPU101954
7322	43506	PAE201359	19384	55568	EBC101285	31445	67629	PPU101976
7323	43507	PAE202724	19385	55569	EBC101287	31446	67630	PPU101981
7324	43508	PAE204241	19386	55570	EBC101290	31447	67631	PPU101984
7325	43509	PAE203520	19387	55571	EBC101291	31448	67632	PPU101987
7326	43510	PAE203119	19388	55572	EBC101294	31449	67633	PPU101997
7327	43511	PAE200320	19389	55573	EBC101295	31450	67634	PPU102000
7328	43512	PAE200028	19390	55574	EBC101303	31451	67635	PPU102004
7329	43513	PAE204244	19391	55575	EBC101305	31452	67636	PPU102022
7330	43514	PAE204245	19392	55576	EBC101306	31453	67637	PPU102025
7331	43515	PAE200881	19393	55577	EBC101308	31454	67638	PPU102030
7332	43516	PAE204596	19394	55578	EBC101311	31455	67639	PPU102034
7333	43517	PAE205311	19395	55579	EBC101317	31456	67640	PPU102036
7334	43518	PAE204260	19396	55580	EBC101321	31457	67641	PPU102041
7335	43519	PAE204078	19397	55581	EBC101322	31458	67642	PPU102045
7336	43520	PAE200649	19398	55582	EBC101332	31459	67643	PPU102062
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7338	43522	PAE200129	19400	55584	EBC101342	31461	67645	PPU102070
7339	43523	PAE204510	19401	55585	EBC101345	31462	67646	PPU102082
7340	43524	PAE201071	19402	55586	EBC101346	31463	67647	PPU102088
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7346	43530	PAE201018	19408	55592	EBC101385	31469	67653	PPU102134
7347	43531	PAE204021	19409	55593	EBC101386	31470	67654	PPU102151
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7357	43541	PAE205194	19419	55603	EBC101417	31480	67664	PPU102184
7358	43542	PAE200418	19420	55604	EBC101418	31481	67665	PPU102190
7359	43543	PAE200417	19421	55605	EBC101419	31482	67666	PPU102196
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7362	43546	PAE105774	19424	55608	EBC101433	31485	67669	PPU102202
7363	43547	PAE203713	19425	55609	EBC101434	31486	67670	PPU102205
7364	43548	PAE205383	19426	55610	EBC101436	31487	67671	PPU102206
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7369	43553	PAE202468	19431	55615	EBC101457	31492	67676	PPU102277
7370	43554	PAE203372	19432	55616	EBC101460	31493	67677	PPU102291
7371	43555	PAE205388	19433	55617	EBC101468	31494	67678	PPU102301
7372	43556	PAE203080	19434	55618	EBC101470	31495	67679	PPU102306
7373	43557	PAE200505	19435	55619	EBC101472	31496	67680	PPU102310
7374	43558	PAE203482	19436	55620	EBC101473	31497	67681	PPU102313
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7376	43560	PAE201916	19438	55622	EBC101476	31499	67683	PPU102385
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7380	43564	PAE200120	19442	55626	EBC101483	31503	67687	PPU102549
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7389	43573	PAE205019	19451	55635	EBC101552	31512	67696	PPU102730
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7983	44167	SAU802241	20045	56229	EBC104020	32106	68290	PPU111360
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8139	44323	SAU802308	20201	56385	EBC107179	32262	68446	PRT100555
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8143	44327	SAU801912	20205	56389	EBC107301	32266	68450	PRT100559
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8306	44490	ABA100008	20368	56552	ECO101483	32429	68613	PRT101447
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8348	44532	ABA100127	20410	56594	ECO102034	32471	68655	PRT101726
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8370	44554	ABA100197	20432	56616	ECO102168	32493	68677	PRT101849
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8408	44592	ABA100380	20470	56654	ECO102629	32531	68715	PRT102108
8409	44593	ABA100381	20471	56655	ECO102667	32532	68716	PRT102120
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8417	44601	ABA100413	20479	56663	ECO102724	32540	68724	PRT102211
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8574	44758	ABA101266	20636	56820	ECO201335	32697	68881	PRT103094
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8580	44764	ABA101297	20642	56826	ECO201939	32703	68887	PRT103160
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8585	44769	ABA101317	20647	56831	ECO203135	32708	68892	PRT103239
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8596	44780	ABA101377	20658	56842	ECO204773	32719	68903	PRT103332
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8635	44819	ABA101674	20697	56881	EFA200173	32758	68942	PRT103877
8636	44820	ABA101677	20698	56882	EFA200188	32759	68943	PRT103889
8637	44821	ABA101702	20699	56883	EFA200190	32760	68944	PRT103897
8638	44822	ABA101710	20700	56884	EFA200191	32761	68945	PRT103903
8639	44823	ABA101740	20701	56885	EFA200193	32762	68946	PRT103927
8640	44824	ABA101766	20702	56886	EFA200201	32763	68947	PRT103939
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8739	44923	ABA103108	20801	56985	EFA200678	32862	69046	PRT104898
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8743	44927	ABA103234	20805	56989	EFA200693	32866	69050	PRT104910
8744	44928	ABA103247	20806	56990	EFA200701	32867	69051	PRT104914
8745	44929	ABA103339	20807	56991	EFA200703	32868	69052	PRT104931
8746	44930	ABA103347	20808	56992	EFA200704	32869	69053	PRT104944
8747	44931	ABA103427	20809	56993	EFA200707	32870	69054	PRT104948
8748	44932	ABA103514	20810	56994	EFA200710	32871	69055	PRT104969
8749	44933	ABA103520	20811	56995	EFA200711	32872	69056	PRT104973
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8751	44935	ABA103540	20813	56997	EFA200715	32874	69058	PRT105013
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8778	44962	ABA103728	20840	57024	EFA200809	32901	69085	PRT105196
8779	44963	ABA103732	20841	57025	EFA200810	32902	69086	PRT105204
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8794	44978	ABA103859	20856	57040	EFA200870	32917	69101	PRT105280
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8799	44983	ABA103932	20861	57045	EFA200895	32922	69106	PRT105312
8800	44984	ABA103937	20862	57046	EFA200896	32923	69107	PRT105337
8801	44985	ABA103947	20863	57047	EFA200904	32924	69108	PRT105340
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8813	44997	ABA104052	20875	57059	EFA201006	32936	69120	PRT105481
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8816	45000	ABA104072	20878	57062	EFA201026	32939	69123	PRT105493
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8823	45007	ABA104108	20885	57069	EFA201059	32946	69130	PRT105522
8824	45008	ABA104125	20886	57070	EFA201062	32947	69131	PRT105528
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8856	45040	ABA104393	20918	57102	EFA201241	32979	69163	PRT105730
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8911	45095	ABA104828	20973	57157	EFA201508	33034	69218	PRT106151
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8948	45132	ABA105088	21010	57194	EFA201668	33071	69255	PSY100343
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8956	45140	ABA105148	21018	57202	EFA201725	33079	69263	PSY100530
8957	45141	ABA105151	21019	57203	EFA201729	33080	69264	PSY100555
8958	45142	ABA105152	21020	57204	EFA201739	33081	69265	PSY100559
8959	45143	ABA105158	21021	57205	EFA201740	33082	69266	PSY100579
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8965	45149	ABA105182	21027	57211	EFA201799	33088	69272	PSY100713
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8967	45151	ABA105190	21029	57213	EFA201804	33090	69274	PSY100720
8968	45152	ABA105195	21030	57214	EFA201808	33091	69275	PSY100727
8969	45153	ABA105202	21031	57215	EFA201809	33092	69276	PSY100737
8970	45154	ABA105208	21032	57216	EFA201812	33093	69277	PSY100759
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8987	45171	ABA105409	21049	57233	EFA201890	33110	69294	PSY100956
8988	45172	ABA105410	21050	57234	EFA201894	33111	69295	PSY100971
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8990	45174	ABA105442	21052	57236	EFA201899	33113	69297	PSY100988
8991	45175	ABA105445	21053	57237	EFA201902	33114	69298	PSY101006
8992	45176	ABA105447	21054	57238	EFA201919	33115	69299	PSY101011
8993	45177	ABA105449	21055	57239	EFA201924	33116	69300	PSY101023
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8997	45181	ABA105477	21059	57243	EFA201933	33120	69304	PSY101033
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9003	45187	ABA105518	21065	57249	EFA201972	33126	69310	PSY101054
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9005	45189	ABA105528	21067	57251	EFA201995	33128	69312	PSY101063
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9009	45193	ABA105537	21071	57255	EFA202014	33132	69316	PSY101078
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9012	45196	ABA105566	21074	57258	EFA202030	33135	69319	PSY101120
9013	45197	ABA105571	21075	57259	EFA202033	33136	69320	PSY101139
9014	45198	ABA105572	21076	57260	EFA202035	33137	69321	PSY101154
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9019	45203	ABA105593	21081	57265	EFA202070	33142	69326	PSY101204
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9026	45210	ABA105638	21088	57272	EFA202092	33149	69333	PSY101227
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9032	45216	ABA105729	21094	57278	EFA202131	33155	69339	PSY101259
9033	45217	ABA105732	21095	57279	EFA202140	33156	69340	PSY101270
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9038	45222	ABA105759	21100	57284	EFA202162	33161	69345	PSY101307
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9048	45232	ABA105807	21110	57294	EFA202219	33171	69355	PSY101350
9049	45233	ABA105815	21111	57295	EFA202220	33172	69356	PSY101352
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9059	45243	ABA105899	21121	57305	EFA202281	33182	69366	PSY101574
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9061	45245	ABA105924	21123	57307	EFA202292	33184	69368	PSY101603
9062	45246	ABA105929	21124	57308	EFA202294	33185	69369	PSY101607
9063	45247	ABA105938	21125	57309	EFA202329	33186	69370	PSY101610
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9065	45249	ABA105948	21127	57311	EFA202331	33188	69372	PSY101651
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9069	45253	ABA105994	21131	57315	EFA202344	33192	69376	PSY101677
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9074	45258	ABA106040	21136	57320	EFA202357	33197	69381	PSY101698
9075	45259	ABA106047	21137	57321	EFA202358	33198	69382	PSY101701
9076	45260	ABA106057	21138	57322	EFA202359	33199	69383	PSY101711
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9078	45262	ABA106059	21140	57324	EFA202362	33201	69385	PSY101745
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9080	45264	ABA106084	21142	57326	EFA202368	33203	69387	PSY101764
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9082	45266	ABA106107	21144	57328	EFA202372	33205	69389	PSY101769
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9114	45298	BAN100191	21176	57360	EFA202691	33237	69421	PSY102145
9115	45299	BAN100193	21177	57361	EFA202706	33238	69422	PSY102146
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9129	45313	BAN100279	21191	57375	EFA203174	33252	69436	PSY102222
9130	45314	BAN100298	21192	57376	EFA203222	33253	69437	PSY102225
9131	45315	BAN100304	21193	57377	EFA203228	33254	69438	PSY102229
9132	45316	BAN100305	21194	57378	EFA203247	33255	69439	PSY102269
9133	45317	BAN100313	21195	57379	EFA203403	33256	69440	PSY102309
9134	45318	BAN100334	21196	57380	EFA203405	33257	69441	PSY102320
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9136	45320	BAN100345	21198	57382	EFA203407	33259	69443	PSY102332
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9144	45328	BAN100388	21206	57390	EFA204183	33267	69451	PSY102383
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9148	45332	BAN100415	21210	57394	EFA204368	33271	69455	PSY102423
9149	45333	BAN100418	21211	57395	EFA204507	33272	69456	PSY102424
9150	45334	BAN100420	21212	57396	EFA204644	33273	69457	PSY102425
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9154	45338	BAN100434	21216	57400	EFA205116	33277	69461	PSY102435
9155	45339	BAN100435	21217	57401	EFA205322	33278	69462	PSY102464
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9157	45341	BAN100446	21219	57403	EFM100074	33280	69464	PSY102492
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9184	45368	BAN100648	21246	57430	EFM100483	33307	69491	PSY102683
9185	45369	BAN100661	21247	57431	EFM100494	33308	69492	PSY102684
9186	45370	BAN100665	21248	57432	EFM100507	33309	69493	PSY102686
9187	45371	BAN100668	21249	57433	EFM100508	33310	69494	PSY102688
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9626	45810	BAN104342	21688	57872	EFM201766	33749	69933	PSY105277
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10993	47177	BBU100513	23055	59239	KPN300325	35116	71300	SHA100146
10994	47178	BBU100517	23056	59240	KPN300326	35117	71301	SHA100148
10995	47179	BBU100527	23057	59241	KPN300330	35118	71302	SHA100151

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10997	47181	BBU100539	23059	59243	KPN300336	35120	71304	SHA100165
10998	47182	BBU100541	23060	59244	KPN300345	35121	71305	SHA100169
10999	47183	BBU100543	23061	59245	KPN300355	35122	71306	SHA100170
11000	47184	BBU100545	23062	59246	KPN300357	35123	71307	SHA100171
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11003	47187	BBU100556	23065	59249	KPN300377	35126	71310	SHA100178
11004	47188	BBU100557	23066	59250	KPN300384	35127	71311	SHA100179
11005	47189	BBU100559	23067	59251	KPN300389	35128	71312	SHA100180
11006	47190	BBU100560	23068	59252	KPN300399	35129	71313	SHA100193
11007	47191	BBU100564	23069	59253	KPN300407	35130	71314	SHA100217
11008	47192	BBU100569	23070	59254	KPN300416	35131	71315	SHA100218
11009	47193	BBU100571	23071	59255	KPN300418	35132	71316	SHA100223
11010	47194	BBU100574	23072	59256	KPN300422	35133	71317	SHA100227
11011	47195	BBU100578	23073	59257	KPN300423	35134	71318	SHA100232
11012	47196	BBU100584	23074	59258	KPN300432	35135	71319	SHA100233
11013	47197	BBU100585	23075	59259	KPN300433	35136	71320	SHA100235
11014	47198	BBU100586	23076	59260	KPN300435	35137	71321	SHA100236
11015	47199	BBU100587	23077	59261	KPN300439	35138	71322	SHA100242
11016	47200	BBU100588	23078	59262	KPN300446	35139	71323	SHA100251
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11025	47209	BBU100614	23087	59271	KPN300484	35148	71332	SHA100292
11026	47210	BBU100615	23088	59272	KPN300488	35149	71333	SHA100294
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11046	47230	BBU100679	23108	59292	KPN300544	35169	71353	SHA100368
11047	47231	BBU100681	23109	59293	KPN300548	35170	71354	SHA100370
11048	47232	BBU100683	23110	59294	KPN300551	35171	71355	SHA100371
11049	47233	BBU100684	23111	59295	KPN300573	35172	71356	SHA100373
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11055	47239	BBU100695	23117	59301	KPN300581	35178	71362	SHA100400
11056	47240	BBU100696	23118	59302	KPN300590	35179	71363	SHA100405
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11061	47245	BBU100709	23123	59307	KPN300609	35184	71368	SHA100415
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11063	47247	BBU100714	23125	59309	KPN300615	35186	71370	SHA100419
11064	47248	BBU100719	23126	59310	KPN300616	35187	71371	SHA100424
11065	47249	BBU100720	23127	59311	KPN300622	35188	71372	SHA100433
11066	47250	BBU100723	23128	59312	KPN300629	35189	71373	SHA100436
11067	47251	BBU100726	23129	59313	KPN300636	35190	71374	SHA100437
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11070	47254	BBU100736	23132	59316	KPN300640	35193	71377	SHA100443
11071	47255	BBU100737	23133	59317	KPN300648	35194	71378	SHA100447
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11073	47257	BBU100753	23135	59319	KPN300650	35196	71380	SHA100451
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11078	47262	BBU100777	23140	59324	KPN300695	35201	71385	SHA100469
11079	47263	BBU100779	23141	59325	KPN300696	35202	71386	SHA100475
11080	47264	BBU100780	23142	59326	KPN300697	35203	71387	SHA100476
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11089	47273	BBU100799	23151	59335	KPN300721	35212	71396	SHA100501
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11102	47286	BBU100832	23164	59348	KPN300812	35225	71409	SHA100548
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11110	47294	BCE100058	23172	59356	KPN300864	35233	71417	SHA100581
11111	47295	BCE100085	23173	59357	KPN300867	35234	71418	SHA100585
11112	47296	BCE100092	23174	59358	KPN300868	35235	71419	SHA100587
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11114	47298	BCE100122	23176	59360	KPN300870	35237	71421	SHA100589
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11116	47300	BCE100189	23178	59362	KPN300872	35239	71423	SHA100595
11117	47301	BCE100228	23179	59363	KPN300875	35240	71424	SHA100600
11118	47302	BCE100234	23180	59364	KPN300876	35241	71425	SHA100601
11119	47303	BCE100247	23181	59365	KPN300879	35242	71426	SHA100602
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11121	47305	BCE100250	23183	59367	KPN300883	35244	71428	SHA100609
11122	47306	BCE100277	23184	59368	KPN300884	35245	71429	SHA100620
11123	47307	BCE100299	23185	59369	KPN300885	35246	71430	SHA100631
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11125	47309	BCE100302	23187	59371	KPN300900	35248	71432	SHA100637
11126	47310	BCE100315	23188	59372	KPN300906	35249	71433	SHA100638
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11129	47313	BCE100404	23191	59375	KPN300926	35252	71436	SHA100641
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11131	47315	BCE100458	23193	59377	KPN300934	35254	71438	SHA100647
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11134	47318	BCE100474	23196	59380	KPN300967	35257	71441	SHA100651
11135	47319	BCE100481	23197	59381	KPN300972	35258	71442	SHA100654
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11144	47328	BCE100650	23206	59390	KPN301039	35267	71451	SHA100689
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11146	47330	BCE100669	23208	59392	KPN301044	35269	71453	SHA100698
11147	47331	BCE100671	23209	59393	KPN301045	35270	71454	SHA100699
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11157	47341	BCE100913	23219	59403	KPN301069	35280	71464	SHA100738
11158	47342	BCE100919	23220	59404	KPN301083	35281	71465	SHA100744
11159	47343	BCE100924	23221	59405	KPN301084	35282	71466	SHA100745
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11165	47349	BCE100976	23227	59411	KPN301102	35288	71472	SHA100764
11166	47350	BCE100985	23228	59412	KPN301109	35289	71473	SHA100765
11167	47351	BCE100989	23229	59413	KPN301110	35290	71474	SHA100766
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11169	47353	BCE101034	23231	59415	KPN301113	35292	71476	SHA100769
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11172	47356	BCE101069	23234	59418	KPN301120	35295	71479	SHA100772
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11177	47361	BCE101166	23239	59423	KPN301139	35300	71484	SHA100778
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11180	47364	BCE101177	23242	59426	KPN301146	35303	71487	SHA100791
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11182	47366	BCE101199	23244	59428	KPN301149	35305	71489	SHA100794
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11206	47390	BCE101479	23268	59452	KPN301276	35329	71513	SHA100866
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11213	47397	BCE101562	23275	59459	KPN301301	35336	71520	SHA100899
11214	47398	BCE101565	23276	59460	KPN301302	35337	71521	SHA100902
11215	47399	BCE101590	23277	59461	KPN301304	35338	71522	SHA100905



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11219	47403	BCE101676	23281	59465	KPN301327	35342	71526	SHA100911
11220	47404	BCE101681	23282	59466	KPN301328	35343	71527	SHA100914
11221	47405	BCE101717	23283	59467	KPN301330	35344	71528	SHA100915
11222	47406	BCE101730	23284	59468	KPN301336	35345	71529	SHA100922
11223	47407	BCE101745	23285	59469	KPN301340	35346	71530	SHA100923
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11225	47409	BCE101777	23287	59471	KPN301346	35348	71532	SHA100928
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11246	47430	BCE102110	23308	59492	KPN301429	35369	71553	SHA100990
11247	47431	BCE102114	23309	59493	KPN301430	35370	71554	SHA100991
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11440	47624	BCE105408	23502	59686	KPN302255	35563	71747	SHA101604			
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11663	47847	BCE109015	23725	59909	KPN303475	35786	71970	SHA102778
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11668	47852	BCE109138	23730	59914	KPN303487	35791	71975	SHA102823
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11673	47857	BCE109237	23735	59919	KPN303513	35796	71980	SHA102869
11674	47858	BCE109252	23736	59920	KPN303514	35797	71981	SHA102882
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12211	48395	BFR101582	24273	60457	LMO100576	36334	72518	SMU101451
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12430	48614	BFR104408	24492	60676	LMO101439	36553	72737	SPA100619
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12432	48616	BFR10442	24494	60678	LMO101445	36555	72739	SPA100621
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12436	48620	BFR104438	24498	60682	LMO101454	36559	72743	SPA100636
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12453	48637	BFR104660	24515	60699	LMO101523	36576	72760	SPA100719
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12539	48723	BFR105965	24601	60785	LMO101852	36662	72846	SPA101091
12540	48724	BFR105970	24602	60786	LMO101855	36663	72847	SPA101093
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13474	49658	BFU107731	25536	61720	MAV101236	37597	73781	SPN400305
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14554	50738	BMA109480	26616	62800	MBV105271	38677	74861	STM100156
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14558	50742	BMA109515	26620	62804	MBV105322	38681	74865	STM100221
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14569	50753	BMA109618	26631	62815	MBV105423	38692	74876	STM100295
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14623	50807	BPT100086	26685	62869	MBV106246	38746	74930	STM100668
14624	50808	BPT100089	26686	62870	MBV106247	38747	74931	STM100673
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14644	50828	BPT100209	26706	62890	MCA100105	38767	74951	STM100933
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14687	50871	BPT100447	26749	62933	MCA100276	38810	74994	STM101289
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14743	50927	BPT100743	26805	62989	MCA100529	38866	75050	STM101689
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14785	50969	BPT100871	26847	63031	MCA100752	38908	75092	STM102069
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DNA SeqID	Protein SeqID	Gene LocusID	DNA SeqID	Protein SeqID	Gene LocusID	DNA SeqID	Protein SeqID	Gene LocusID
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14792	50976	BPT100891	26854	63038	MCA100772	38915	75099	STM102138
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14794	50978	BPT100893	26856	63040	MCA100777	38917	75101	STM102148
14795	50979	BPT100894	26857	63041	MCA100778	38918	75102	STM102165
14796	50980	BPT100895	26858	63042	MCA100779	38919	75103	STM102169
14797	50981	BPT100896	26859	63043	MCA100780	38920	75104	STM102195
14798	50982	BPT100897	26860	63044	MCA100781	38921	75105	STM102200
14799	50983	BPT100902	26861	63045	MCA100787	38922	75106	STM102205
14800	50984	BPT100905	26862	63046	MCA100789	38923	75107	STM102228
14801	50985	BPT100907	26863	63047	MCA100794	38924	75108	STM102230
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14803	50987	BPT100913	26865	63049	MCA100801	38926	75110	STM102232
14804	50988	BPT100915	26866	63050	MCA100802	38927	75111	STM102234
14805	50989	BPT100922	26867	63051	MCA100805	38928	75112	STM102243
14806	50990	BPT100924	26868	63052	MCA100807	38929	75113	STM102259
14807	50991	BPT100926	26869	63053	MCA100812	38930	75114	STM102262
14808	50992	BPT100929	26870	63054	MCA100816	38931	75115	STM102273
14809	50993	BPT100934	26871	63055	MCA100818	38932	75116	STM102277
14810	50994	BPT100938	26872	63056	MCA100819	38933	75117	STM102282
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14812	50996	BPT100941	26874	63058	MCA100821	38935	75119	STM102306
14813	50997	BPT100944	26875	63059	MCA100829	38936	75120	STM102307
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14821	51005	BPT100971	26883	63067	MCA100866	38944	75128	STM102429
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14832	51016	BPT101009	26894	63078	MCA100916	38955	75139	STM102603
14833	51017	BPT101013	26895	63079	MCA100917	38956	75140	STM102604
14834	51018	BPT101024	26896	63080	MCA100918	38957	75141	STM102620
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14836	51020	BPT101027	26898	63082	MCA100934	38959	75143	STM102670
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14842	51026	BPT101079	26904	63088	MCA100961	38965	75149	STM102718
14843	51027	BPT101088	26905	63089	MCA100969	38966	75150	STM102719
14844	51028	BPT101104	26906	63090	MCA100972	38967	75151	STM102720
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14850	51034	BPT101112	26912	63096	MCA101000	38973	75157	STM102728
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14855	51039	BPT101121	26917	63101	MCA101005	38978	75162	STM102761
14856	51040	BPT101128	26918	63102	MCA101007	38979	75163	STM102772
14857	51041	BPT101129	26919	63103	MCA101008	38980	75164	STM102778
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14864	51048	BPT101147	26926	63110	MCA101062	38987	75171	STM102815
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14866	51050	BPT101152	26928	63112	MCA101080	38989	75173	STM102828
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14887	51071	BPT101318	26949	63133	MCA101150	39010	75194	STM102893
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14897	51081	BPT101374	26959	63143	MCA101187	39020	75204	STM102974
14898	51082	BPT101378	26960	63144	MCA101190	39021	75205	STM103004
14899	51083	BPT101379	26961	63145	MCA101196	39022	75206	STM103008
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14906	51090	BPT101398	26968	63152	MCA101231	39029	75213	STM103130
14907	51091	BPT101402	26969	63153	MCA101238	39030	75214	STM103140
14908	51092	BPT101404	26970	63154	MCA101240	39031	75215	STM103141
14909	51093	BPT101405	26971	63155	MCA101241	39032	75216	STM103144
14910	51094	BPT101412	26972	63156	MCA101243	39033	75217	STM103149
14911	51095	BPT101413	26973	63157	MCA101251	39034	75218	STM103155
14912	51096	BPT101418	26974	63158	MCA101252	39035	75219	STM103167
14913	51097	BPT101420	26975	63159	MCA101253	39036	75220	STM103175
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14916	51100	BPT101434	26978	63162	MCA101274	39039	75223	STM103181
14917	51101	BPT101439	26979	63163	MCA101278	39040	75224	STM103197
14918	51102	BPT101441	26980	63164	MCA101289	39041	75225	STM103199
14919	51103	BPT101443	26981	63165	MCA101313	39042	75226	STM103201
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14972	51156	BPT101777	27034	63218	MCA101622	39095	75279	STM103587
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14974	51158	BPT101787	27036	63220	MCA101636	39097	75281	STM103592
14975	51159	BPT101790	27037	63221	MCA101639	39098	75282	STM103593
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14977	51161	BPT101799	27039	63223	MCA101641	39100	75284	STM103598
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14979	51163	BPT101805	27041	63225	MCA101652	39102	75286	STM103613
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15003	51187	BPT101957	27065	63249	MCA101910	39126	75310	STM103807
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15005	51189	BPT101965	27067	63251	MCA101940	39128	75312	STM103821
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15007	51191	BPT101969	27069	63253	MCA101946	39130	75314	STM103861
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15009	51193	BPT101987	27071	63255	MCA101962	39132	75316	STM103910
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15013	51197	BPT102003	27075	63259	MCA101980	39136	75320	STM103922
15014	51198	BPT102004	27076	63260	MCA101981	39137	75321	STM103926
15015	51199	BPT102027	27077	63261	MCA101987	39138	75322	STM103952
15016	51200	BPT102032	27078	63262	MCA101994	39139	75323	STM103969
15017	51201	BPT102034	27079	63263	MCA101998	39140	75324	STM104010
15018	51202	BPT102039	27080	63264	MCA102001	39141	75325	STM104011
15019	51203	BPT102040	27081	63265	MCA102006	39142	75326	STM104015
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15248	51432	BPT104317	27310	63494	MGE100180	39371	75555	STY101082
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15714	51898	CAC102285	27776	63960	MLP101137	39837	76021	STY103176
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15716	51900	CAC102294	27778	63962	MLP101139	39839	76023	STY103179
15717	51901	CAC102305	27779	63963	MLP101140	39840	76024	STY103182
15718	51902	CAC102306	27780	63964	MLP101141	39841	76025	STY103207
15719	51903	CAC102314	27781	63965	MLP101142	39842	76026	STY103209
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15722	51906	CAC102331	27784	63968	MLP101145	39845	76029	STY103214
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15724	51908	CAC102336	27786	63970	MLP101148	39847	76031	STY103217
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15733	51917	CAC102383	27795	63979	MLP101184	39856	76040	STY103282
15734	51918	CAC102388	27796	63980	MLP101190	39857	76041	STY103289
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15739	51923	CAC102421	27801	63985	MLP101197	39862	76046	STY103303
15740	51924	CAC102428	27802	63986	MLP101198	39863	76047	STY103321
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15742	51926	CAC102434	27804	63988	MLP101209	39865	76049	STY103325
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15745	51929	CAC102460	27807	63991	MLP101237	39868	76052	STY103330
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15747	51931	CAC102468	27809	63993	MLP101243	39870	76054	STY103378
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15778	51962	CAC102622	27840	64024	MLP101401	39901	76085	STY103505
15779	51963	CAC102623	27841	64025	MLP101416	39902	76086	STY103507
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15784	51968	CAC102647	27846	64030	MLP101437	39907	76091	STY103516
15785	51969	CAC102648	27847	64031	MLP101438	39908	76092	STY103518
15786	51970	CAC102661	27848	64032	MLP101439	39909	76093	STY103526
15787	51971	CAC102666	27849	64033	MLP101453	39910	76094	STY103547
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15791	51975	CAC102676	27853	64037	MLP101478	39914	76098	STY103566
15792	51976	CAC102682	27854	64038	MLP101480	39915	76099	STY103588
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15799	51983	CAC102712	27861	64045	MLP101538	39922	76106	STY103641
15800	51984	CAC102718	27862	64046	MLP101539	39923	76107	STY103643
15801	51985	CAC102721	27863	64047	MLP101542	39924	76108	STY103649
15802	51986	CAC102729	27864	64048	MLP101543	39925	76109	STY103659
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15824	52008	CAC102804	27886	64070	MPN100010	39947	76131	STY103809
15825	52009	CAC102810	27887	64071	MPN100031	39948	76132	STY103811
15826	52010	CAC102817	27888	64072	MPN100032	39949	76133	STY103813
15827	52011	CAC102832	27889	64073	MPN100037	39950	76134	STY103815
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15830	52014	CAC102862	27892	64076	MPN100048	39953	76137	STY103824
15831	52015	CAC102864	27893	64077	MPN100049	39954	76138	STY103825
15832	52016	CAC102868	27894	64078	MPN100067	39955	76139	STY103826
15833	52017	CAC102879	27895	64079	MPN100073	39956	76140	STY103840
15834	52018	CAC102880	27896	64080	MPN100074	39957	76141	STY103841
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15839	52023	CAC102906	27901	64085	MPN100082	39962	76146	STY103852
15840	52024	CAC102908	27902	64086	MPN100083	39963	76147	STY103853
15841	52025	CAC102909	27903	64087	MPN100084	39964	76148	STY103856
15842	52026	CAC102921	27904	64088	MPN100087	39965	76149	STY103858
15843	52027	CAC102924	27905	64089	MPN100088	39966	76150	STY103859
15844	52028	CAC102927	27906	64090	MPN100090	39967	76151	STY103862
15845	52029	CAC102930	27907	64091	MPN100091	39968	76152	STY103864
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15847	52031	CAC102940	27909	64093	MPN100094	39970	76154	STY103871
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15851	52035	CAC102955	27913	64097	MPN100104	39974	76158	STY103879
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15856	52040	CAC102981	27918	64102	MPN100111	39979	76163	STY103901
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15889	52073	CAC103154	27951	64135	MPN100205	40012	76196	STY103994
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15895	52079	CAC103184	27957	64141	MPN100219	40018	76202	STY104020
15896	52080	CAC103197	27958	64142	MPN100220	40019	76203	STY104022
15897	52081	CAC103209	27959	64143	MPN100223	40020	76204	STY104029
15898	52082	CAC103216	27960	64144	MPN100224	40021	76205	STY104030
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15917	52101	CAC103337	27979	64163	MPN100284	40040	76224	STY104152
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15919	52103	CAC103360	27981	64165	MPN100286	40042	76226	STY104154
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15928	52112	CAC103422	27990	64174	MPN100326	40051	76235	STY104173
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15930	52114	CAC103441	27992	64176	MPN100346	40053	76237	STY104177
15931	52115	CAC103450	27993	64177	MPN100347	40054	76238	STY104182
15932	52116	CAC103453	27994	64178	MPN100348	40055	76239	STY104185
15933	52117	CAC103455	27995	64179	MPN100352	40056	76240	STY104186
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15936	52120	CAC103481	27998	64182	MPN100365	40059	76243	STY104192
15937	52121	CAC103483	27999	64183	MPN100366	40060	76244	STY104199
15938	52122	CAC103488	28000	64184	MPN100367	40061	76245	STY104200
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15941	52125	CAC103503	28003	64187	MPN100388	40064	76248	STY104209
15942	52126	CAC103515	28004	64188	MPN100395	40065	76249	STY104213
15943	52127	CAC103516	28005	64189	MPN100397	40066	76250	STY104221
15944	52128	CAC103521	28006	64190	MPN100407	40067	76251	STY104231
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15948	52132	CAC103561	28010	64194	MPN100414	40071	76255	STY104247
15949	52133	CAC103563	28011	64195	MPN100415	40072	76256	STY104257
15950	52134	CAC103566	28012	64196	MPN100416	40073	76257	STY104266
15951	52135	CAC103575	28013	64197	MPN100417	40074	76258	STY104272
15952	52136	CAC103585	28014	64198	MPN100419	40075	76259	STY104274
15953	52137	CAC103586	28015	64199	MPN100420	40076	76260	STY104276
15954	52138	CAC103600	28016	64200	MPN100421	40077	76261	STY104279
15955	52139	CAC103602	28017	64201	MPN100422	40078	76262	STY104286
15956	52140	CAC103604	28018	64202	MPN100427	40079	76263	STY104295
15957	52141	CAC103605	28019	64203	MPN100430	40080	76264	STY104298
15958	52142	CAC103617	28020	64204	MPN100432	40081	76265	STY104302
15959	52143	CAC103620	28021	64205	MPN100436	40082	76266	STY104305
15960	52144	CAC103630	28022	64206	MPN100441	40083	76267	STY104319
15961	52145	CAC103631	28023	64207	MPN100445	40084	76268	STY104329
15962	52146	CAC103641	28024	64208	MPN100446	40085	76269	STY104331
15963	52147	CAC103650	28025	64209	MPN100447	40086	76270	STY104333
15964	52148	CAC103652	28026	64210	MPN100448	40087	76271	STY104335
15965	52149	CAC103654	28027	64211	MPN100453	40088	76272	STY104336
15966	52150	CAC103664	28028	64212	MPN100457	40089	76273	STY104340
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15969	52153	CAC103679	28031	64215	MPN100475	40092	76276	STY104356
15970	52154	CAC103684	28032	64216	MPN100476	40093	76277	STY104366
15971	52155	CAC103685	28033	64217	MPN100479	40094	76278	STY104382
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15973	52157	CAC103696	28035	64219	MPN100482	40096	76280	STY104391
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15976	52160	CAC103721	28038	64222	MPN100486	40099	76283	STY104427
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15978	52162	CAC103735	28040	64224	MPN100488	40101	76285	STY104449
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15998	52182	CBO100064	28060	64244	MPN100522	40121	76305	STY104545
15999	52183	CBO100087	28061	64245	MPN100526	40122	76306	STY104553
16000	52184	CBO100089	28062	64246	MPN100528	40123	76307	STY104558

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16010	52194	CBO100154	28072	64256	MPN100558	40133	76317	STY104578
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16016	52200	CBO100202	28078	64262	MPN100578	40139	76323	STY104593
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16028	52212	CBO100249	28090	64274	MPN100603	40151	76335	STY104820
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16061	52245	CBO100415	28123	64307	MPN100654	40184	76368	TPA100028
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16066	52250	CBO100441	28128	64312	MPN100659	40189	76373	TPA100051
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16068	52252	CBO100452	28130	64314	MPN100661	40191	76375	TPA100055
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16070	52254	CBO100465	28132	64316	MPN100663	40193	76377	TPA100057
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16116	52300	CBO100775	28178	64362	MTU200278	40239	76423	TPA100195
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16162	52346	CBO101000	28224	64408	MTU200635	40285	76469	TPA100300
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16164	52348	CBO101009	28226	64410	MTU200637	40287	76471	TPA100303
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16171	52355	CBO101032	28233	64417	MTU200671	40294	76478	TPA100337
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16208	52392	CBO101216	28270	64454	MTU200806	40331	76515	TPA100471
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16445	52629	CBO102689	28507	64691	MTU202299	40568	76752	UUR100210
16446	52630	CBO102699	28508	64692	MTU202300	40569	76753	UUR100211
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16452	52636	CBO102727	28514	64698	MTU202325	40575	76759	UUR100229
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16462	52646	CBO102797	28524	64708	MTU202392	40585	76769	UUR100239
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16476	52660	CBO102943	28538	64722	MTU202439	40599	76783	UUR100253
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16500	52684	CBO103041	28562	64746	MTU202546	40623	76807	UUR100310
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16604	52788	CBO103642	28666	64850	MTU203187	40727	76911	UUR100577
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16619	52803	CBO103707	28681	64865	MTU203289	40742	76926	UUR100601
16620	52804	CBO103711	28682	64866	MTU203293	40743	76927	UUR100602
16621	52805	CBO103715	28683	64867	MTU203301	40744	76928	UUR100603
16622	52806	CBO103725	28684	64868	MTU203321	40745	76929	UUR100606
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16630	52814	CBO103765	28692	64876	MTU203377	40753	76937	VCH100007
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16640	52824	CBO103826	28702	64886	MTU203412	40763	76947	VCH100040
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16650	52834	CBO103874	28712	64896	MTU203462	40773	76957	VCH100108
16651	52835	CBO103886	28713	64897	MTU203475	40774	76958	VCH100112
16652	52836	CBO103893	28714	64898	MTU203523	40775	76959	VCH100120
16653	52837	CBO103904	28715	64899	MTU203528	40776	76960	VCH100127
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16658	52842	CBO103931	28720	64904	MTU203540	40781	76965	VCH100138
16659	52843	CBO103935	28721	64905	MTU203543	40782	76966	VCH100146
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16664	52848	CBO103956	28726	64910	MTU203558	40787	76971	VCH100165
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16668	52852	CDF100007	28730	64914	MTU203575	40791	76975	VCH100185
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16671	52855	CDF100018	28733	64917	MTU203605	40794	76978	VCH100194
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16703	52887	CDF100130	28765	64949	MTU203863	40826	77010	VCH100321
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16723	52907	CDF100237	28785	64969	MTU401062	40846	77030	VCH100384
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16775	52959	CDF100458	28837	65021	NGO100099	40898	77082	VCH100549
16776	52960	CDF100459	28838	65022	NGO100106	40899	77083	VCH100550
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16800	52984	CDF100548	28862	65046	NGO100201	40923	77107	VCH100626
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16824	53008	CDF100692	28886	65070	NGO100300	40947	77131	VCH100685
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16831	53015	CDF100729	28893	65077	NGO100339	40954	77138	VCH100723
16832	53016	CDF100733	28894	65078	NGO100345	40955	77139	VCH100726
16833	53017	CDF100735	28895	65079	NGO100361	40956	77140	VCH100728
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16869	53053	CDF100863	28931	65115	NGO100553	40992	77176	VCH100893
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16956	53140	CDF101218	29018	65202	NGO100888	41079	77263	VCH101281
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16997	53181	CDF101445	29059	65243	NGO100995	41120	77304	VCH101565
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17052	53236	CDF101760	29114	65298	NGO101218	41175	77359	VCH101890
17053	53237	CDF101762	29115	65299	NGO101220	41176	77360	VCH101891
17054	53238	CDF101764	29116	65300	NGO101240	41177	77361	VCH101899
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17539	53723	CDP100250	29601	65785	NME200684	41662	77846	YPS000696
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17931	54115	CDP101620	29993	66177	PAE200454	42054	78238	YPS002292
17932	54116	CDP101627	29994	66178	PAE200458	42055	78239	YPS002296
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17979	54163	CDP101991	30041	66225	PAE200902	42102	78286	YPS002494
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17996	54180	CDP102443	30058	66242	PAE201038	42119	78303	YPS002552
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18025	54209	CJU100021	30087	66271	PAE201317	42148	78332	YPS002675
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18046	54230	CJU100094	30108	66292	PAE201520	42169	78353	YPS002805
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18191	54375	CJU100575	30253	66437	PAE202976	42314	78498	YPS003414
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18197	54381	CJU100594	30259	66443	PAE203027	42320	78504	YPS003425
18198	54382	CJU100600	30260	66444	PAE203032	42321	78505	YPS003432
18199	54383	CJU100601	30261	66445	PAE203042	42322	78506	YPS003443
18200	54384	CJU100602	30262	66446	PAE203081	42323	78507	YPS003446

DNA SeqID	Protein SeqID	Gene LocusID	DNA SeqID	Protein SeqID	Gene LocusID	DNA SeqID	Protein SeqID	Gene LocusID
18201	54385	CJU100605	30263	66447	PAE203086	42324	78508	YPS003447
18202	54386	CJU100617	30264	66448	PAE203102	42325	78509	YPS003448
18203	54387	CJU100619	30265	66449	PAE203103	42326	78510	YPS003452
18204	54388	CJU100620	30266	66450	PAE203110	42327	78511	YPS003454
18205	54389	CJU100622	30267	66451	PAE203113	42328	78512	YPS003458
18206	54390	CJU100624	30268	66452	PAE203114	42329	78513	YPS003462
18207	54391	CJU100628	30269	66453	PAE203132	42330	78514	YPS003466
18208	54392	CJU100629	30270	66454	PAE203139	42331	78515	YPS003469
18209	54393	CJU100636	30271	66455	PAE203146	42332	78516	YPS003474
18210	54394	CJU100638	30272	66456	PAE203155	42333	78517	YPS003477
18211	54395	CJU100643	30273	66457	PAE203160	42334	78518	YPS003478
18212	54396	CJU100645	30274	66458	PAE203161	42335	78519	YPS003483
18213	54397	CJU100646	30275	66459	PAE203166	42336	78520	YPS003494
18214	54398	CJU100649	30276	66460	PAE203177	42337	78521	YPS003496
18215	54399	CJU100651	30277	66461	PAE203193	42338	78522	YPS003498
18216	54400	CJU100654	30278	66462	PAE203199	42339	78523	YPS003500
18217	54401	CJU100659	30279	66463	PAE203203	42340	78524	YPS003502
18218	54402	CJU100660	30280	66464	PAE203206	42341	78525	YPS003510
18219	54403	CJU100661	30281	66465	PAE203208	42342	78526	YPS003517
18220	54404	CJU100662	30282	66466	PAE203256	42343	78527	YPS003520
18221	54405	CJU100663	30283	66467	PAE203264	42344	78528	YPS003522
18222	54406	CJU100664	30284	66468	PAE203270	42345	78529	YPS003528
18223	54407	CJU100668	30285	66469	PAE203277	42346	78530	YPS003531
18224	54408	CJU100669	30286	66470	PAE203294	42347	78531	YPS003539
18225	54409	CJU100672	30287	66471	PAE203299	42348	78532	YPS003542
18226	54410	CJU100675	30288	66472	PAE203301	42349	78533	YPS003544
18227	54411	CJU100684	30289	66473	PAE203302	42350	78534	YPS003545
18228	54412	CJU100698	30290	66474	PAE203303	42351	78535	YPS003546
18229	54413	CJU100702	30291	66475	PAE203331	42352	78536	YPS003547
18230	54414	CJU100704	30292	66476	PAE203342	42353	78537	YPS003552
18231	54415	CJU100705	30293	66477	PAE203357	42354	78538	YPS003553
18232	54416	CJU100709	30294	66478	PAE203386	42355	78539	YPS003556
18233	54417	CJU100710	30295	66479	PAE203414	42356	78540	YPS003559
18234	54418	CJU100711	30296	66480	PAE203415	42357	78541	YPS003562
18235	54419	CJU100712	30297	66481	PAE203450	42358	78542	YPS003580
18236	54420	CJU100714	30298	66482	PAE203457	42359	78543	YPS003605
18237	54421	CJU100728	30299	66483	PAE203459	42360	78544	YPS003633
18238	54422	CJU100729	30300	66484	PAE203468	42361	78545	YPS003640
18239	54423	CJU100732	30301	66485	PAE203480	42362	78546	YPS003644
18240	54424	CJU100734	30302	66486	PAE203501	42363	78547	YPS003651
18241	54425	CJU100735	30303	66487	PAE203514	42364	78548	YPS003677
18242	54426	CJU100737	30304	66488	PAE203515	42365	78549	YPS003683
18243	54427	CJU100740	30305	66489	PAE203525	42366	78550	YPS003696
18244	54428	CJU100741	30306	66490	PAE203552	42367	78551	YPS003702
18245	54429	CJU100742	30307	66491	PAE203556	42368	78552	YPS003731
18246	54430	CJU100744	30308	66492	PAE203557	42369	78553	YPS003739
18247	54431	CJU100749	30309	66493	PAE203558	42370	78554	YPS003752
18248	54432	CJU100751	30310	66494	PAE203560	42371	78555	YPS003775
18249	54433	CJU100756	30311	66495	PAE203565	42372	78556	YPS003777
18250	54434	CJU100760	30312	66496	PAE203579	42373	78557	YPS003792
18251	54435	CJU100763	30313	66497	PAE203580	42374	78558	YPS003815
18252	54436	CJU100766	30314	66498	PAE203588	42375	78559	YPS003822
18253	54437	CJU100774	30315	66499	PAE203595	42376	78560	YPS003891
18254	54438	CJU100775	30316	66500	PAE203599	42377	78561	YPS003904
18255	54439	CJU100777	30317	66501	PAE203600	42378	78562	YPS003930



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DNA SeqID	Protein SeqID	Gene LocusID	DNA SeqID	Protein SeqID	Gene LocusID	DNA SeqID	Protein SeqID	Gene LocusID
18256	54440	CJU100788	30318	66502	PAE203601	42379	78563	YPS003983
18257	54441	CJU100795	30319	66503	PAE203612	42380	78564	YPS004039
18258	54442	CJU100797	30320	66504	PAE203614	42381	78565	YPS004144
18259	54443	CJU100799	30321	66505	PAE203615	42382	78566	YPS004146
18260	54444	CJU100801	30322	66506	PAE203618	42383	78567	YPS004171
18261	54445	CJU100802	30323	66507	PAE203625	42384	78568	YPS004196
18262	54446	CJU100805	30324	66508	PAE203626	42385	78569	YPS004197
18263	54447	CJU100815	30325	66509	PAE203631	42386	78570	YPS004214
18264	54448	CJU100816	30326	66510	PAE203633	42387	78571	YPS004281
18265	54449	CJU100817	30327	66511	PAE203634	42388	78572	YPS004286
18266	54450	CJU100819	30328	66512	PAE203635	42389	78573	YPS004652
18267	54451	CJU100824	30329	66513	PAE203637	42390	78574	YPS005092
18268	54452	CJU100827	30330	66514	PAE203638	42391	78575	YPS005095
18269	54453	CJU100828	30331	66515	PAE203640	42392	78576	YPS005126
18270	54454	CJU100833	30332	66516	PAE203643	42393	78577	YPS005201
18271	54455	CJU100835	30333	66517	PAE203644	42394	78578	YPS005574
18272	54456	CJU100836	30334	66518	PAE203650	42395	78579	YPS005860
18273	54457	CJU100842	30335	66519	PAE203651	42396	78580	YPS006083
18274	54458	CJU100843	30336	66520	PAE203652	42397	78581	YPS006344
18275	54459	CJU100845						

It will be appreciated that ORFs may also be identified using databases other than PathoSeq. For example, the ORFs may be identified using the methods described in U.S. Provisional Patent Application Serial Number 60/191,078, filed March 21, 2000.

#### EXAMPLE 4

##### 5      Transfer of Exogenous Nucleic Acid Sequences to other Bacterial Species

The ability of an antisense molecule identified in a first organism to inhibit the proliferation of a second organism (thereby confirming that a gene in the second organism which is homologous to the gene from the first organism is required for proliferation of the second organism) was validated using antisense nucleic acids which inhibit the growth of *E. coli* which were identified using methods similar to those described above. Expression vectors which inhibited growth of *E. coli* upon induction of antisense RNA expression with IPTG were transformed directly into *Enterobacter cloacae*, *Klebsiella pneumoniae* or *Salmonella typhimurium*. The transformed cells were then assayed for growth inhibition according to the method of Example 1. After growth in liquid culture, cells were plated at various serial dilutions and a score determined by calculating the log difference in growth for INDUCED vs. UNINDUCED antisense RNA expression as determined by the maximum 10 fold dilution at which a colony was observed. The results of these experiments are listed below in Table II. If there was no effect of antisense RNA expression in a microorganism, the clone is minus in Table II. In contrast, a positive in Table II means that at least 10 fold more cells were required to observe a colony on the induced plate than on the non-induced plate under the conditions used and in that microorganism.

TABLE II  
Sensitivity of Other Microorganisms to Antisense Nucleic Acids That Inhibit Proliferation in *E. coli*

Mol. No.	<i>S. typhimurium</i>	<i>E. cloacae</i>	<i>K. pneumoniae</i>
EcXA001	+	+	-
EcXA004	+	-	-
EcXA005	+	+	+
EcXA006	-	-	-
EcXA007	-	+	-
EcXA008	+	-	+
EcXA009	-	-	-
EcXA010	+	+	+
EcXA011	-	+	-
EcXA012	-	+	-
EcXA013	+	+	+
EcXA014	+	+	-
EcXA015	+	+	+
EcXA016	+	+	+
EcXA017	+	+	+
EcXA018	+	+	+
EcXA019	+	+	+
EcXA020	+	+	+
EcXA021	+	+	+
EcXA023	+	+	+
EcXA024	+	-	+

EcXA025	-	-	-
EcXA026	+	+	-
EcXA027	+	+	-
EcXA028	+	-	-
EcXA029	-	-	-
EcXA030	+	+	+
EcXA031	+	-	-
EcXA032	+	+	-
EcXA033	+	+	+
EcXA034	+	+	+
EcXA035	-	-	-
EcXA036	+	-	+
EcXA037	+	+	-
EcXA038	+	+	+
EcXA039	+	-	-
EcXA041	+	+	+
EcXA042	-	+	+
EcXA043	-	-	-
EcXA044	-	-	-
EcXA045	+	+	+
EcXA046	-	-	-
EcXA047	+	+	-
EcXA048	-	-	-
EcXA049	+	-	-
EcXA050	-	-	-
EcXA051	+	-	-
EcXA052	+	-	-
EcXA053	+	+	+
EcXA054	-	-	+
EcXA055	+	-	-
EcXA056	+	-	+
EcXA057	+	+	-
EcXA058	-	-	-
EcXA059	+	+	+
EcXA060	-	-	-
EcXA061	-	-	-
EcXA062	-	-	-
EcXA063	+	+	-
EcXA064	-	-	-
EcXA065	+	+	-
EcXA066	-	-	-
EcXA067	-	+	-
EcXA068	-	-	-
EcXA069	-	+	-
EcXA070	-	-	-
EcXA071	+	-	-
EcXA072	+	-	+
EcXA073	+	+	+
EcXA074	+	+	+
EcXA075	+	-	-
EcXA076	-	+	-

EcXA077	+	+	-
EcXA079	+	+	+
EcXA080	+	-	-
EcXA082	-	+	-
EcXA083	-	-	-
EcXA084	-	+	-
EcXA086	-	-	-
EcXA087	-	-	-
EcXA088	-	-	-
EcXA089	-	-	-
EcXA090	-	-	-
EcXA091	-	-	-
EcXA092	-	-	-
EcXA093	-	-	-
EcXA094	+	+	+
EcXA095	+	+	-
EcXA096	-	-	-
EcXA097	+	-	-
EcXA098	+	-	-
EcXA099	-	-	-
EcXA100	-	-	-
EcXA101	-	-	-
EcXA102	-	-	-
EcXA103	-	+	-
EcXA104	+	+	+
EcXA106	+	+	-
EcXA107	-	-	-
EcXA108	-	-	-
EcXA109	-	-	-
EcXA110	+	+	-
EcXA111	-	-	-
EcXA112	-	+	-
EcXA113	+	+	+
EcXA114	-	+	-
EcXA115	-	+	-
EcXA116	+	+	-
EcXA117	+	-	-
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EcXA119	+	+	-
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EcXA122	+	-	+
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EcXA126	-	-	-
EcXA127	+	+	-
EcXA128	-	-	-
EcXA129	-	+	-
EcXA130	+	+	-
EcXA132	-	-	-

EcXA133	-	-	-
EcXA136	-	-	-
EcXA137	-	-	-
EcXA138	+	-	-
EcXA139	-	-	-
EcXA140	+	-	-
EcXA141	+	-	-
EcXA142	-	-	-
EcXA143	-	+	-
EcXA144	+	+	-
EcXA145	-	-	-
EcXA146	-	-	-
EcXA147	-	-	-
EcXA148	-	-	-
EcXA149	+	+	+
EcXA150	-	-	-
EcXA151	+	-	-
EcXA152	-	-	-
EcXA153	+	+	-
EcXA154	-	-	-
EcXA155	-	-	ND
EcXA156	-	+	-
EcXA157	-	-	-
EcXA158	-	-	-
EcXA159	+	-	-
EcXA160	+	-	-
EcXA162	-	-	-
EcXA163	-	-	-
EcXA164	-	-	-
EcXA165	-	-	-
EcXA166	-	-	-
EcXA167	-	-	-
EcXA168	-	-	-
EcXA169	-	+	-
EcXA171	-	-	-
EcXA172	-	-	-
EcXA173	-	-	-
EcXA174	-	-	-
EcXA175	-	-	-
EcXA176	-	-	-
EcXA178	-	-	-
EcXA179	-	-	-
EcXA180	+	-	-
EcXA181	-	-	-
EcXA182	-	-	-
EcXA183	-	-	-
EcXA184	-	-	-
EcXA185	-	-	-
EcXA186	-	-	-
EcXA187	+	+	+
EcXA189	+	-	-

EcXA190	+	+	+
EcXA191	+	+	-
EcXA192	-	+	-

Thus, the ability of an antisense nucleic acid which inhibits the proliferation of *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*,  
5 *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae* or *Yersinia pestis* to inhibit the growth of other organisms may be  
10 evaluated by transforming the antisense nucleic acid directly into species other than the organism from which they were obtained. In particular, the ability of the antisense nucleic acid to inhibit the growth of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*,  
20 *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*,  
25 *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*,  
30 *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*,  
35 *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma*

*urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* or any species falling within the genera of any of the above species may be evaluated. In some embodiments of the present invention, the ability of the antisense nucleic acid to inhibit the growth of an organism other than *E. coli* may be evaluated. In such embodiments, the antisense nucleic acids are inserted into expression vectors functional in the organisms in which the antisense nucleic acids are evaluated.

It will be appreciated that the above methods for evaluating the ability of an antisense nucleic acid to inhibit the proliferation of a heterologous organism may be performed using antisense nucleic acids complementary to any of the proliferation-required nucleic acids from *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae* or *Yersinia pestis* (including antisense nucleic acids complementary to SEQ ID NOs.: 6214-42397, such as the antisense nucleic acids of SEQ ID NOs.: 1-6213) or portions thereof, antisense nucleic acids complementary to homologous coding nucleic acids or portions thereof, or homologous antisense nucleic acids.

Those skilled in the art will appreciate that a negative result in a heterologous cell or microorganism does not mean that that cell or microorganism is missing that gene nor does it mean that the gene is unessential. However, a positive result means that the heterologous cell or microorganism contains a homologous gene which is required for proliferation of that cell or microorganism. The homologous gene may be obtained using the methods described herein. For example, the homologous gene may be isolated by performing a PCR procedure using primers based on the antisense sequence which reduced the level or activity of the gene product encoded by the homologous gene or by performing a Southern blot. Those cells that are inhibited by antisense may be used in cell-based assays as described herein for the identification and characterization of compounds in order to develop antibiotics effective in these cells or microorganisms. Those skilled in the art will appreciate that an antisense molecule which works in the microorganism from which it was obtained will not always work in a heterologous cell or microorganism.

## EXAMPLE 5

Transfer of Exogenous Nucleic Acid Sequences to Other Bacterial Species Using the *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae* or *Yersinia pestis* Expression Vectors or Expression Vectors Functional in Bacterial Species Other Than the Foregoing Bacterial Species

The antisense nucleic acids that inhibit the growth of *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae* or *Yersinia pestis*, or portions thereof, may also be evaluated for their ability to inhibit the growth of cells or microorganisms other than *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*,



*Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae* or *Yersinia pestis*. For example, the antisense nucleic acids that inhibit the growth of *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae* or *Yersinia pestis* may be evaluated for their ability to inhibit the growth of other organisms. In particular, the ability of the antisense nucleic acid to inhibit the growth of *Acinetobacter baumannii*, *Anaplasma marginale*, *Aspergillus fumigatus*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Candida albicans*, *Candida glabrata* (also called *Torulopsis glabrata*), *Candida tropicalis*, *Candida parapsilosis*, *Candida guilliermondii*, *Candida krusei*, *Candida kefyr* (also called *Candida pseudotropicalis*), *Candida dubliniensis*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Coccidioides immitis*, *Corynebacterium diphtheriae*, *Cryptococcus neoformans*, *Enterobacter cloacae*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Haemophilus influenzae*, *Helicobacter pylori*, *Histoplasma capsulatum*, *Klebsiella pneumoniae*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Nocardia asteroides*, *Pasteurella haemolytica*, *Pasteurella multocida*, *Pneumocystis carinii*, *Proteus mirabilis*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella bongori*, *Salmonella choleraesuis*, *Salmonella enterica*, *Salmonella paratyphi*, *Salmonella typhi*, *Salmonella typhimurium*, *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*,

*Streptococcus pneumoniae*, *Streptococcus mutans*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Vibrio vulnificans*, *Yersinia enterocolitica*, *Yersinia pestis* or any species falling within the genera of any of the above species may be evaluated. In some embodiments of the present invention, the ability of the antisense nucleic acid to inhibit the growth of an organism other than *E. coli* may be evaluated.

In such methods, expression vectors in which the expression of an antisense nucleic acid that inhibits the growth of *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae* or *Yersinia pestis* under the control of an inducible promoter are introduced into the cells or microorganisms in which they are to be evaluated. In some embodiments, the antisense nucleic acids may be evaluated in cells or microorganisms which are closely related to *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae* or *Yersinia pestis*. The ability of these antisense nucleic acids to inhibit the growth of the related cells or microorganisms in the presence of the inducer is then measured.

#### EXAMPLE 6

Identification of Nucleic Acids Homologous to Nucleic Acids Required for the Proliferation of

*Staphylococcus aureus* in other Bacterial Species

Nucleic acids homologous to proliferation-required nucleic acids from *Staphylococcus aureus* were identified as follows. For example, thirty-nine antisense nucleic acids which inhibited the growth of *Staphylococcus aureus* were identified using methods such as those described herein and were inserted into an expression vector such that their expression was under the control of a xylose-inducible Xyl-T5 promoter. A vector with a reporter gene under control of the Xyl-T5 promoter was used to show that expression from the Xyl-T5 promoter in *Staphylococcus epidermidis* was comparable to that in *Staphylococcus aureus*.

The vectors were introduced into *Staphylococcus epidermidis* by electroporation as follows: *Staphylococcus epidermidis* was grown in liquid culture to mid-log phase and then harvested by centrifugation. The cell pellet was resuspended in 1/3 culture volume of ice-cold EP buffer (0.625 M sucrose, 1 mM MgCl<sub>2</sub>, pH=4.0), and then harvested again by centrifugation. The cell pellet was then resuspended with 1/40 volume EP buffer and allowed to incubate on ice for 1 hour. The cells were then frozen for storage at -80°C. For electroporation, 50 µl of thawed electrocompetent cells were combined with 0.5 µg plasmid DNA and then subjected to an electrical pulse of 10 kV/cm, 25 uFarads, 200 ohm using a biorad gene pulser electroporation device. The cells were immediately resuspended with 200 µl outgrowth medium and incubated for 2 hours prior to plating on solid growth medium with drug selection to maintain the plasmid vector. Colonies resulting from overnight growth of these platings were selected, cultured in liquid medium with drug selection, and then subjected to dilution plating analysis as described for *Staphylococcus aureus* in Example 1 above to test growth sensitivity in the presence of the inducer xylose.

The results are shown in Table III below. The first column indicates the Molecule Number of the *Staphylococcus aureus* antisense nucleic acid which was introduced into *Staphylococcus epidermidis*. The second column indicates whether the antisense nucleic acid inhibited the growth of *Staphylococcus epidermidis*, with a "+" indicating that growth was inhibited. Of the 39 *Staphylococcus aureus* antisense nucleic acids evaluated, 20 inhibited the growth of *Staphylococcus epidermidis*.

**TABLE III**  
Sensitivity of Other Microorganisms to Antisense Nucleic Acids That Inhibit Proliferation of  
*Staphylococcus aureus*

Mol. No.	<i>S. epidermidis</i>
SaXA005	+
SaXA007	+
SaXA008	+
SaXA009	+
SaXA010	+
SaXA011	-

SaXA012	-
SaXA013	-
SaXA015	+
SaXA017	-
SaXA022	+
SaXA023	-
SaXA024	-
SaXA025	+
SaXA026	+
SaXA027	-
SaXA027b	-
SaXA02c	-
SaXA028	-
SaXA029	+
SaXA030	+
SaXA032	+
SaXA033	+
SaXA034	-
SaXA035	+
SaXA037	+
SaXA039	-
SaXA042	-
SaXA043	-
SaXA044	-
SaXA045	+
SaXA051	+
SaXA053	-
SaXA056b	-
SaXA059a	+
SaXA060	-
SaXA061	+
SaXA062	+
SaXA063	-
SaXA065	-

Although the results shown above were obtained using a subset of proliferation-required nucleic acids from *Staphylococcus aureus*, it will be appreciated that similar analyses may be performed using the nucleic acids of the present invention to determine whether they inhibit the proliferation of cells or microorganisms other than *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae* or *Yersinia pestis*.

Thus, it will be appreciated that the above methods for evaluating the ability of an antisense nucleic acid to inhibit the proliferation of a heterologous organism may be performed using antisense nucleic acids complementary to any of the proliferation-required nucleic acids from *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae* or *Yersinia pestis*, (including antisense nucleic acids complementary to SEQ ID NOs.: 6214-42397, such as the antisense nucleic acids of SEQ ID NOs.: 1-6213) or portions thereof, antisense nucleic acids complementary to homologous coding nucleic acids or portions thereof, or homologous antisense nucleic acids.

## EXAMPLE 7

Identification of Homologous Nucleic Acids by Functional Complementation

Homologous coding nucleic acids, homologous antisense nucleic acids or nucleic acids encoding homologous polypeptides may be identified as follows. Gene products whose activities

5 may be complemented by a proliferation-required gene product from *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*,

10 *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella*

15 *multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae*, *Yersinia pestis* or homologous polypeptides are identified using merodiploids, created by introducing a plasmid or Bacterial Artificial Chromosome into an

20 organism having a mutation in the essential gene which reduces or eliminates the activity of the gene product. In some embodiments, the mutation may be a conditional mutation, such as a temperature sensitive mutation, such that the organism proliferates under permissive conditions but is unable to proliferate under non-permissive conditions in the absence of complementation by the gene on the plasmid or Bacterial Artificial Chromosome. Alternatively, duplications may be

25 constructed as described in Roth et al. (1987) Biosynthesis of Aromatic Amino Acids in *Escherichia coli* and *Salmonella typhimurium*, F. C. Neidhardt, ed., American Society for Microbiology, publisher, pp. 2269-2270. Such methods are familiar to those skilled in the art. Alternatively, homologous coding nucleic acids, homologous antisense nucleic acids or nucleic acids encoding homologous polypeptides may be identified by placing a gene required for

30 proliferation or a nucleic acid complementary to at least a portion of a gene required for proliferation under the control of a regulatable promoter as described above, introducing a plasmid or Bacterial Artificial Chromosome into the cell, and identifying cells which are able to proliferate under conditions which would prevent or reduce proliferation in the absence of the plasmid or Bacterial Artificial Chromosome.

35 Homologous coding nucleic acids, homologous antisense nucleic acids or nucleic acids encoding homologous polypeptides may be identified using databases as follows.

## EXAMPLE 8

Identification of Homologous Nucleic Acids by Database Analysis

As a demonstration of the methodology required to find homologues to an essential gene, fifty-one prokaryotic organisms were analyzed and compared in detail. First, the most reliable source of gene sequences for each organism was assessed by conducting a survey of the public and private data sources. The fifty-one organisms studied are *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Salmonella typhimurium*, *Acinetobacter baumannii*, *Bacillus anthracis*, *Bacteroides fragilis*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Burkholderia cepacia*, *Burkholderia fungorum*, *Burkholderia mallei*, *Campylobacter jejuni*, *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Clostridium acetobutylicum*, *Clostridium botulinum*, *Clostridium difficile*, *Corynebacterium diphtheriae*, *Enterobacter cloacae*, *Enterococcus faecium*, *Haemophilus influenzae*, *Helicobacter pylori*, *Legionella pneumophila*, *Listeria monocytogenes*, *Moraxella catarrhalis*, *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium leprae*, *Mycobacterium tuberculosis*, *Mycoplasma genitalium*, *Mycoplasma pneumoniae*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Pasteurella multocida*, *Proteus mirabilis*, *Pseudomonas putida*, *Pseudomonas syringae*, *Salmonella paratyphi*, *Salmonella typhi*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, *Streptococcus mutans*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Treponema pallidum*, *Ureaplasma urealyticum*, *Vibrio cholerae* and *Yersinia pestis*. Full-length gene protein and nucleotide sequences for these organisms were assembled from various sources. For *Escherichia coli*, *Haemophilus influenzae* and *Helicobacter pylori*, gene sequences were adopted from the public sequencing projects, and derived from the GenPept 115 database (available from NCBI). For *Pseudomonas aeruginosa*, gene sequences were adopted from the *Pseudomonas* genome sequencing project (downloaded from <http://www.pseudomonas.com>). For *Klebsiella pneumoniae*, *Staphylococcus aureus*, *Streptococcus pneumoniae* and *Salmonella typhi*, genomic sequences from PathoSeq v 4.1 (Mar 2000 release) were reanalyzed for ORFs using the gene finding software GeneMark v 2.4a, which was purchased from GenePro Inc. 451 Bishop St., N.W., Suite B, Atlanta, GA, 30318, USA. Similar analyses were conducted for the other organisms using publically available and proprietary databases.

Homologous coding nucleic acids and the homologous polypeptides which they encode may be identified using a "reciprocal" best-hit analysis. To facilitate the identification of homologous coding nucleic acids and homologous polypeptides, paralogous genes within each of 51 organisms were identified and clustered prior to comparison to other organisms. Briefly, the polypeptide sequence of each polypeptide encoded by each open reading frame (ORF) in a given organism was compared to the polypeptide sequence encoded by every other ORF for that organism for each of the 51 pathogenic organisms (PathoSeq Sept 2001 release) using BLASTP 2.09 algorithm without filtering. Simultaneously, the polypeptide sequence encoded by each ORF of an organism was compared to the polypeptide sequences encoded by each of the ORFs in the remaining 51 organisms. Those polypeptides within a single organism that shared a higher degree

of sequence identity to one another than to polypeptide sequences obtained from any other organisms were clustered as "paralog" sequences for "reciprocal" best-hit analysis.

For each reference organism, the 50 homologous coding nucleic acids (and the 50 homologous polypeptides which they encode) was determined by identifying the ORFs in each of the 50 comparison organisms which encode a polypeptide sharing the highest degree of amino acid sequence identity to the polypeptide encoded by the ORF from the reference organism. The accuracy of the identification of the predicted homologous coding nucleic acids (and the homologous polypeptides which they encode) was confirmed by a "reciprocal" BLAST analysis in which the polypeptide sequence of the predicted homologous polypeptide was compared against the polypeptides encoded by each of the ORFS in the reference organism using BLASTP 2.09 algorithm without filtering. Only those polypeptides that share the highest degree of amino acid sequence identity in each portion of the two-way comparison are retained for further analysis.

The best homolog for each of the fifty-one organisms, defined as the most significantly scoring match which also fulfilled the above criteria, was reported in Table IV.

Table IV lists the best ORF identified as described above (column labeled Homolog LocusID) that matches the query sequence (column labeled Query LocusID), % identity between the query sequence and the homolog, and the amount of each sequence that aligns together well (columns labeled Query Coverage and Homolog Coverage) for the gene identified in each of the fifty-one organisms evaluated as described above. As described in connection with Table IC, the Locus IDs (ie. both Query Locus ID and Homolog Locus ID) provided in Table IV each comprise a nine digit alpha-numeric identifier that can be used to determine the organism from which the query and homolog sequences were obtained. Specifically, the first letter of the Locus ID corresponds to the first letter of the genus name of the organism described herein from which the Locus was identified and the second and third letters of the Locus ID correspond to the first two letters of the species name of this organism. For example, the identifier EFA205257 describes a gene locus identified from *Enterococcus faecalis*. In those instances where the three letter identifier is the same for different organisms, the exact identity of the organism which corresponds to the Locus ID can be determined by referring to the organism designation in the sequence listing for the coding nucleic acid or polypeptide SEQ ID NO. that corresponds to the particular Locus ID.



TABLE IV

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100001	ECO100001	100%	100%	100%
ECO100001	STY104800	85%	100%	100%
ECO100001	STM104529	85%	100%	100%
ECO100002	ABA101891	29%	40.9%	80.3%
ECO100002	BAN108126	29%	55.5%	98.5%
ECO100002	BAN105795	30%	55.5%	95.8%
ECO100002	BFR11028	36%	98.9%	99.4%
ECO100002	BPT101425	30%	41.5%	81.7%
ECO100002	BCE111633	28%	42.2%	73.4%
ECO100002	BMA100957	30%	41.3%	82.5%
ECO100002	CJU100543	30%	55.5%	97.8%
ECO100002	CDF100035	25%	5.4%	74.4%
ECO100002	CDF100673	25%	54.9%	96.7%
ECO100002	CDP101634	28%	46.1%	95.7%
ECO100002	EBC103170	92%	70.7%	100%
ECO100002	EFA201386	27%	56.2%	99.8%
ECO100002	ECO100002	100%	100%	100%
ECO100002	HIN100088	62%	99.3%	99.8%
ECO100002	HPY101212	32%	41.8%	83.5%
ECO100002	KPN300246	90%	4.1%	76.7%
ECO100002	KPN302085	92%	100%	100%
ECO100002	LMO102676	27%	57.3%	100%
ECO100002	MCA100888	30%	40.9%	80.3%
ECO100002	MAV103162	26%	55.5%	94.8%
ECO100002	MBV103584	28%	41.0%	79.6%
ECO100002	MLP101383	25%	55.5%	94.8%
ECO100002	MTU203655	28%	41.0%	79.6%
ECO100002	NGO100216	30%	8.9%	4.2%
ECO100002	NME201560	30%	8.9%	4.2%
ECO100002	PMU100113	64%	99.3%	99.8%
ECO100002	PRT104264	76%	100%	100%
ECO100002	PAE200903	30%	4.5%	5.6%
ECO100002	PPU106924	31%	40.9%	80.3%
ECO100002	PSY103112	30%	31.7%	82.0%
ECO100002	SPA100167	93%	39.5%	100%
ECO100002	STY100365	94%	100%	100%
ECO100002	STM100038	94%	100%	100%
ECO100002	SAU801327	26%	56.2%	97.6%
ECO100002	SEP201977	26%	56.2%	98.0%
ECO100002	SHA100755	26%	56.2%	99.8%
ECO100002	SMU100555	25%	56.6%	100%
ECO100002	SPN400374	25%	56.1%	98.7%
ECO100002	VCH102329	62%	100%	99.3%
ECO100002	YPS000769	81%	100%	100%
ECO100004	BFR11030	47%	85.3%	93.3%
ECO100004	BPT101337	32%	99.8%	99.4%
ECO100004	BCE114764	28%	97.4%	96.9%
ECO100004	BFU101149	29%	94.9%	94.6%
ECO100004	BMA105857	30%	90.4%	95.0%
ECO100004	CJU100751	29%	90.2%	87.2%
ECO100004	CAC103481	28%	99.5%	95.8%
ECO100004	CBO101914	30%	79.9%	86.5%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100004	CDF101928	31%	87.9%	85.6%
ECO100004	CDP100440	27%	99.3%	97.9%
ECO100004	EBC102668	92%	80.1%	100%
ECO100004	ECO100004	100%	100%	100%
ECO100004	HIN100086	66%	99.3%	99.5%
ECO100004	HPY100096	28%	89.3%	86.0%
ECO100004	KPN302095	90%	99.3%	99.8%
ECO100004	LPN102575	35%	89.7%	89.8%
ECO100004	MCA103682	29%	99.1%	98.5%
ECO100004	NGO101188	28%	99.1%	98.9%
ECO100004	NME201311	29%	99.1%	98.9%
ECO100004	PMU100115	69%	99.3%	99.8%
ECO100004	PRT104738	78%	99.3%	98.8%
ECO100004	PAE203732	33%	99.8%	98.5%
ECO100004	PPU107824	35%	93.9%	93.2%
ECO100004	PSY103804	34%	99.8%	98.5%
ECO100004	SPA100998	88%	57.0%	100%
ECO100004	STY100371	93%	100%	100%
ECO100004	STM100044	93%	100%	100%
ECO100004	SMU101311	31%	90.0%	87.2%
ECO100004	SPN401875	32%	90.2%	87.7%
ECO100004	VCH102327	68%	99.5%	99.5%
ECO100004	YPS000771	83%	99.3%	99.1%
ECO100005	BCE106023	30%	67.3%	35.5%
ECO100005	BFU106225	33%	74.5%	90.3%
ECO100005	BMA105475	31%	61.2%	52.5%
ECO100005	EBC102669	57%	99.0%	100%
ECO100005	ECO100005	100%	100%	100%
ECO100005	MAV107742	38%	53.1%	50.6%
ECO100005	PAE109842	33%	55.1%	23.9%
ECO100008	BPT101198	53%	98.7%	98.1%
ECO100008	BCE112831	56%	99.7%	90.3%
ECO100008	BFU112516	57%	99.7%	99.7%
ECO100008	BMA101518	57%	98.7%	98.7%
ECO100008	CJU100252	27%	55.2%	49.8%
ECO100008	EBC102672	94%	100%	100%
ECO100008	ECO100008	100%	100%	100%
ECO100008	HIN101098	79%	98.7%	98.7%
ECO100008	HPY101474	28%	58.4%	57.9%
ECO100008	KPN302087	91%	100%	100%
ECO100008	NME201973	31%	47.0%	41.9%
ECO100008	PMU101639	74%	97.8%	98.1%
ECO100008	PMU101602	77%	98.7%	98.7%
ECO100008	PRT104596	86%	100%	100%
ECO100008	PAE202794	60%	97.8%	97.7%
ECO100008	PPU101750	60%	99.4%	99.4%
ECO100008	PSY102944	60%	98.7%	98.4%
ECO100008	SPA100585	92%	62.1%	100%
ECO100008	STY100380	94%	100%	100%
ECO100008	STM100053	94%	100%	100%
ECO100008	SAU504318	30%	30.6%	17.8%
ECO100008	VCH103346	75%	98.7%	98.7%
ECO100008	YPS000773	88%	100%	100%
ECO100009	BPT100950	69%	96.4%	88.9%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100009	BCE102933	73%	96.4%	95.0%
ECO100009	BFU100752	72%	95.4%	88.1%
ECO100009	BMA109380	72%	96.4%	93.2%
ECO100009	CJU100675	50%	95.9%	97.2%
ECO100009	CAC100345	41%	79.5%	90.3%
ECO100009	CBO103886	42%	79.5%	92.0%
ECO100009	CDF101203	35%	78.5%	88.6%
ECO100009	EBC102673	90%	98.5%	98.5%
ECO100009	EFA202344	45%	71.3%	83.8%
ECO100009	ECO100009	100%	100%	100%
ECO100009	HIN100319	79%	96.9%	95.9%
ECO100009	HPY100786	48%	95.9%	99.4%
ECO100009	KPN302084	91%	98.5%	98.5%
ECO100009	MAV104045	37%	75.9%	91.9%
ECO100009	MBV100298	33%	75.9%	90%
ECO100009	MTU200856	33%	75.9%	90%
ECO100009	PMU102003	78%	96.4%	97.9%
ECO100009	PRT105678	82%	99.5%	99.5%
ECO100009	SPA100586	93%	98.5%	98.0%
ECO100009	STY100383	93%	98.5%	98.0%
ECO100009	STM100056	91%	98.5%	98.0%
ECO100009	YPS000774	87%	100%	100%
ECO100013	ECO100013	100%	100%	100%
ECO100013	KPN302079	66%	98.5%	100%
ECO100013	SPA105546	80%	100%	100%
ECO100013	STY106203	82%	100%	100%
ECO100023	ABA106150	60%	92.0%	67.2%
ECO100023	BAN103797	50%	96.6%	95.5%
ECO100023	BFR105539	39%	100%	100%
ECO100023	BPT101291	51%	100%	100%
ECO100023	BBU100232	38%	92.0%	74.8%
ECO100023	BCE112030	47%	98.9%	95.6%
ECO100023	BFU100359	51%	98.9%	93.5%
ECO100023	BMA106459	48%	98.9%	93.5%
ECO100023	CJU101517	34%	100%	100%
ECO100023	CPN201099	31%	94.3%	82.8%
ECO100023	CTR200896	33%	88.5%	75.5%
ECO100023	CAC102146	45%	98.9%	97.7%
ECO100023	CBO100245	39%	98.9%	97.7%
ECO100023	CDF101197	41%	96.6%	81.6%
ECO100023	CDP101196	47%	100%	100%
ECO100023	EBC101439	96%	70.1%	100%
ECO100023	EFA200336	48%	92.0%	95.2%
ECO100023	EFM201993	34%	97.7%	100%
ECO100023	ECO100023	100%	100%	100%
ECO100023	HIN100944	72%	100%	97.8%
ECO100023	HPY100074	33%	100%	97.8%
ECO100023	KPN205579	98%	100%	100%
ECO100023	LMO100322	46%	97.7%	100%
ECO100023	MCA100794	56%	98.9%	97.7%
ECO100023	MAV103835	43%	98.9%	100%
ECO100023	MBV104427	41%	98.9%	97.7%
ECO100023	MLP100381	41%	98.9%	100%
ECO100023	MTU202376	43%	98.9%	100%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100023	MGE100374	30%	97.7%	88.6%
ECO100023	MPN100301	31%	97.7%	89.7%
ECO100023	NGO101642	57%	100%	100%
ECO100023	NME201868	57%	100%	100%
ECO100023	PMU101659	78%	100%	97.8%
ECO100023	PRT102018	83%	98.9%	100%
ECO100023	PAE204561	59%	100%	95.6%
ECO100023	PPU108230	59%	98.9%	93.5%
ECO100023	PSY102689	58%	100%	94.6%
ECO100023	SPA101944	97%	100%	100%
ECO100023	STY101095	97%	100%	100%
ECO100023	SAU801586	40%	90.8%	94.0%
ECO100023	SEP203256	37%	90.8%	90.7%
ECO100023	SHA102295	39%	90.8%	94.0%
ECO100023	SMU102606	41%	97.7%	92.9%
ECO100023	SPN400740	43%	97.7%	94.0%
ECO100023	SPY200946	45%	95.4%	98.7%
ECO100023	UUR100312	40%	88.5%	83.3%
ECO100023	VCH100666	70%	98.9%	100%
ECO100023	YPS003605	87%	98.9%	98.9%
ECO100025	ABA101842	41%	97.8%	97.3%
ECO100025	BAN106284	28%	98.1%	99.4%
ECO100025	BAN101499	35%	99.4%	97.2%
ECO100025	BFR100412	36%	98.4%	98.1%
ECO100025	BPT100434	47%	93.3%	93.1%
ECO100025	BCE109423	47%	98.1%	89.0%
ECO100025	BFU101232	45%	98.1%	92.7%
ECO100025	BMA109546	46%	98.1%	89.0%
ECO100025	CJU100550	26%	91.4%	91.9%
ECO100025	CPN200431	31%	92.0%	90.9%
ECO100025	CTR200362	32%	91.1%	93.9%
ECO100025	CAC102490	31%	89.8%	92.4%
ECO100025	CBO102062	31%	86.3%	97.8%
ECO100025	CDF100874	34%	95.5%	94.8%
ECO100025	CDP100453	30%	94.9%	90.1%
ECO100025	EBC100241	84%	56.9%	98.9%
ECO100025	EFA200587	31%	94.9%	94.3%
ECO100025	EFM201219	33%	97.1%	97.4%
ECO100025	ECO100025	100%	100%	100%
ECO100025	HIN100942	53%	98.1%	98.1%
ECO100025	HPY101070	30%	91.4%	93.6%
ECO100025	KPN300577	86%	91.1%	100%
ECO100025	LPN101116	45%	97.8%	92.7%
ECO100025	LMO100570	34%	92.3%	92.0%
ECO100025	MCA100302	41%	93.3%	93.8%
ECO100025	MAV100301	35%	92.0%	93.5%
ECO100025	MBV101247	35%	91.7%	98.4%
ECO100025	MLP100513	36%	91.7%	91.2%
ECO100025	MTU202748	35%	92.0%	91.5%
ECO100025	MGE100147	28%	89.5%	92.9%
ECO100025	MPN100673	27%	92.0%	96.7%
ECO100025	NGO101768	47%	97.1%	95.3%
ECO100025	NME200577	47%	97.1%	95.6%
ECO100025	PMU101661	58%	98.1%	98.4%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100025	PRT105259	67%	97.8%	97.8%
ECO100025	PAE204559	55%	98.1%	98.1%
ECO100025	PPU105777	52%	97.1%	95.9%
ECO100025	PSY102686	52%	97.1%	99.7%
ECO100025	SPA101946	88%	98.7%	100%
ECO100025	STY101100	89%	98.7%	98.7%
ECO100025	STM100815	89%	98.7%	98.7%
ECO100025	SAU801272	34%	97.1%	95.4%
ECO100025	SEP201565	35%	98.7%	96.9%
ECO100025	SHA100170	35%	97.1%	95.4%
ECO100025	SMU100956	36%	91.4%	92.5%
ECO100025	SPN401017	33%	92.0%	93.4%
ECO100025	SPY200960	32%	96.8%	96.1%
ECO100025	TPA100878	30%	69.6%	80%
ECO100025	UUR100357	26%	87.2%	86.9%
ECO100025	VCH100668	58%	97.1%	94.1%
ECO100025	YPS000809	75%	99.7%	99.7%
ECO100026	ABA103852	54%	99.8%	100%
ECO100026	BAN106248	37%	92.3%	96.1%
ECO100026	BAN106209	43%	86.5%	99.1%
ECO100026	BFR10500	25%	81.1%	79.2%
ECO100026	BPT100432	51%	99.5%	99.6%
ECO100026	BBU100832	26%	81.8%	74.0%
ECO100026	BCE111670	51%	95.3%	97.0%
ECO100026	BFU101230	51%	99.3%	98.4%
ECO100026	BMA102496	43%	98.5%	94.9%
ECO100026	BMA109115	50%	99.6%	98.7%
ECO100026	CJU100989	40%	96.3%	97.4%
ECO100026	CPN200653	26%	81.7%	73.5%
ECO100026	CTR200283	27%	81.0%	73.4%
ECO100026	CAC102765	27%	90.5%	81.7%
ECO100026	CBO100873	30%	55.1%	96.8%
ECO100026	CDF104554	29%	80.0%	72.4%
ECO100026	CDP101247	28%	89.1%	80.5%
ECO100026	EBC102151	92%	98.2%	100%
ECO100026	EFA202160	44%	98.1%	97.8%
ECO100026	EFM201425	44%	98.5%	98.1%
ECO100026	ECO100026	100%	100%	100%
ECO100026	HPY101401	39%	98.5%	99.2%
ECO100026	KPN300290	95%	4.7%	100%
ECO100026	KPN306610	92%	98.3%	100%
ECO100026	LPN101832	55%	99.9%	99.9%
ECO100026	LMO101679	43%	98.7%	99.2%
ECO100026	MCA103671	52%	0.9%	16.5%
ECO100026	MAV103388	27%	83.7%	74.6%
ECO100026	MBV102555	28%	82.3%	75.3%
ECO100026	MLP100743	24%	89.0%	80.8%
ECO100026	MTU201515	28%	82.3%	75.3%
ECO100026	MGE100354	32%	98.3%	99.4%
ECO100026	MPN100322	33%	89.3%	95.7%
ECO100026	NGO101799	53%	99.7%	100%
ECO100026	NME200578	53%	100%	100%
ECO100026	PMU101662	69%	99.8%	99.7%
ECO100026	PRT101657	80%	100%	100%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100026	PAE204558	57%	100%	100%
ECO100026	PPU109898	56%	100%	100%
ECO100026	PSY102684	54%	98.3%	100%
ECO100026	SPA100667	85%	82.8%	99.5%
ECO100026	STY101103	86%	100%	100%
ECO100026	STM100818	87%	100%	100%
ECO100026	SAU801193	42%	98.3%	99.0%
ECO100026	SEP200928	42%	98.3%	98.7%
ECO100026	SHA101034	41%	98.2%	99.5%
ECO100026	SMU100109	40%	98.5%	98.1%
ECO100026	SPN401501	41%	98.5%	98.1%
ECO100026	SPY201164	42%	95.8%	95.2%
ECO100026	TPA100448	26%	89.6%	81.1%
ECO100026	UUR100414	36%	97.0%	97.8%
ECO100026	VCH100669	67%	100%	100%
ECO100026	YPS000810	83%	100%	100%
ECO100032	BFR102496	39%	97.6%	100%
ECO100032	BCE114725	66%	97.1%	94.6%
ECO100032	BFU101987	64%	97.1%	90.0%
ECO100032	BMA105964	64%	97.1%	94.6%
ECO100032	CJU101410	40%	96.9%	99.5%
ECO100032	CAC100686	41%	96.3%	99.1%
ECO100032	CDF102200	42%	96.3%	98.8%
ECO100032	CDF101392	47%	97.1%	95.3%
ECO100032	CDP100339	45%	98.2%	94.4%
ECO100032	EBC100940	91%	51.8%	100%
ECO100032	EFA201091	45%	97.9%	98.6%
ECO100032	EFM201379	47%	96.9%	97.8%
ECO100032	ECO100032	100%	100%	100%
ECO100032	HPY101220	38%	97.1%	99.2%
ECO100032	KPN306459	80%	100%	100%
ECO100032	LPN100982	58%	97.6%	99.2%
ECO100032	LMO100114	46%	96.6%	96.1%
ECO100032	MCA101274	62%	96.6%	95.9%
ECO100032	MAV103355	43%	98.2%	99.2%
ECO100032	MBV100477	44%	57.6%	97.3%
ECO100032	MLP100326	42%	98.7%	100%
ECO100032	MTU201366	45%	97.6%	98.7%
ECO100032	NGO101672	67%	96.1%	96.6%
ECO100032	NME200564	67%	97.1%	97.6%
ECO100032	PMU101502	65%	97.1%	95.3%
ECO100032	PRT101652	81%	99.2%	97.9%
ECO100032	PAE204754	71%	99.0%	100%
ECO100032	PPU108522	70%	89.8%	100%
ECO100032	PSY107482	68%	64.4%	100%
ECO100032	SPA101379	86%	100%	100%
ECO100032	STY101157	93%	100%	100%
ECO100032	STM100872	94%	100%	100%
ECO100032	SAU801202	45%	97.6%	96.4%
ECO100032	SEP102450	43%	99.2%	98.1%
ECO100032	SHA102129	44%	99.2%	98.1%
ECO100032	SMU100787	43%	97.6%	97.2%
ECO100032	SPN401153	43%	98.2%	98.6%
ECO100032	SPY200619	43%	98.7%	98.9%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100032	VCH102355	82%	99.0%	99.7%
ECO100032	YPS000843	86%	99.7%	97.4%
ECO100033	ABA105447	76%	86.5%	51.8%
ECO100033	BAN106466	36%	92.5%	93.4%
ECO100033	BAN106013	50%	97.2%	73.8%
ECO100033	BFR11696	39%	96.3%	96.2%
ECO100033	BFR10760	40%	39.0%	91.4%
ECO100033	BPT101199	69%	97.1%	73.7%
ECO100033	BCE101906	68%	99.9%	99.9%
ECO100033	BFU114502	68%	99.9%	99.9%
ECO100033	BMA100194	68%	99.9%	99.9%
ECO100033	CJU100250	55%	100%	99.9%
ECO100033	CAC100380	46%	100%	100%
ECO100033	CDF103346	45%	68.9%	81.0%
ECO100033	CDF103290	48%	97.4%	97.7%
ECO100033	CDF102440	47%	97.4%	97.7%
ECO100033	CDP100338	52%	98.4%	98.2%
ECO100033	EBC103143	96%	4.1%	77.8%
ECO100033	EFA201093	49%	98.6%	99.4%
ECO100033	EFM200554	48%	98.6%	99.4%
ECO100033	ECO100033	100%	100%	100%
ECO100033	HPY100903	53%	99.4%	99.7%
ECO100033	KPN306727	95%	92.1%	92.8%
ECO100033	LPN103124	72%	90.9%	74.6%
ECO100033	LMO101147	50%	98.8%	98.5%
ECO100033	MCA101278	70%	99.7%	99.9%
ECO100033	MAV103356	51%	99.9%	99.4%
ECO100033	MBV100481	52%	99.9%	99.6%
ECO100033	MLP100327	51%	99.9%	98.3%
ECO100033	MTU301470	52%	99.9%	99.6%
ECO100033	NGO101630	69%	100%	99.7%
ECO100033	NME200558	69%	100%	99.7%
ECO100033	PMU101505	69%	99.9%	99.9%
ECO100033	PRT101651	90%	100%	99.8%
ECO100033	PAE204752	76%	100%	99.9%
ECO100033	PPU105037	74%	100%	99.6%
ECO100033	PSY104746	75%	100%	99.9%
ECO100033	SPA101378	93%	87.4%	63.3%
ECO100033	STY101163	98%	100%	99.8%
ECO100033	STM100875	98%	100%	99.8%
ECO100033	SAU801203	49%	99.5%	100%
ECO100033	SEP201467	52%	86.8%	35.4%
ECO100033	SHA102130	49%	99.5%	100%
ECO100033	SMU100789	50%	98.4%	99.2%
ECO100033	SPN401152	49%	98.4%	99.2%
ECO100033	SPY200620	49%	98.4%	99.2%
ECO100033	VCH102354	85%	100%	99.6%
ECO100033	YPS000846	92%	100%	99.6%
ECO100040	ECO100040	100%	100%	100%
ECO100040	MAV102307	26%	22.0%	44.2%
ECO100040	PRT105337	87%	100%	100%
ECO100040	SPA102043	92%	54.8%	100%
ECO100040	STY101185	96%	100%	99.8%
ECO100068	BPT100719	25%	79.8%	77.4%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100068	BCE110446	23%	97.2%	89.3%
ECO100068	BFU104253	25%	59.3%	49.6%
ECO100068	CJU100163	23%	81.0%	82.0%
ECO100068	EBC103044	90%	96.0%	97.5%
ECO100068	ECO100068	100%	100%	100%
ECO100068	HIN100998	50%	99.1%	99.7%
ECO100068	KPN303934	83%	100%	100%
ECO100068	MCA100722	24%	85.6%	85.2%
ECO100068	NGO101933	30%	97.9%	97.3%
ECO100068	NME200270	29%	97.9%	97.3%
ECO100068	PMU100376	49%	95.4%	94.3%
ECO100068	PRT100202	66%	93.9%	94.5%
ECO100068	PAE204684	26%	81.7%	79.7%
ECO100068	PSY105429	22%	88.4%	87.8%
ECO100068	SPA101253	89%	100%	100%
ECO100068	STY101259	91%	100%	100%
ECO100068	TPA100143	31%	91.4%	90.7%
ECO100068	VCH102502	65%	97.6%	97.0%
ECO100068	YPS000940	72%	98.8%	97.9%
ECO100069	BAN110716	37%	7.8%	66.2%
ECO100069	BAN110657	27%	12.0%	60.6%
ECO100069	BAN101932	26%	57.5%	56.3%
ECO100069	EBC103045	79%	100%	100%
ECO100069	ECO100069	100%	100%	100%
ECO100069	KPN303932	78%	100%	100%
ECO100069	LMO101504	24%	94.4%	91.4%
ECO100069	PRT103304	47%	54.3%	100%
ECO100069	SPA101254	81%	99.5%	100%
ECO100069	STY101261	86%	100%	100%
ECO100069	STM100598	38%	99.5%	99.7%
ECO100069	VCH103302	33%	99.5%	99.1%
ECO100069	YPS000941	62%	99.8%	99.8%
ECO100081	BFR12308	32%	53.9%	68.6%
ECO100081	BPT103032	44%	87.5%	90.8%
ECO100081	BCE103942	47%	82.9%	85.9%
ECO100081	BFU100820	48%	82.2%	85.2%
ECO100081	BMA105750	47%	82.2%	85.2%
ECO100081	CAC103463	29%	100%	100%
ECO100081	CBO101902	31%	91.4%	85.9%
ECO100081	CDP101285	34%	93.4%	95.8%
ECO100081	EBC101941	95%	78.9%	100%
ECO100081	EFA202186	34%	88.2%	92.3%
ECO100081	EFM202534	39%	82.2%	83.9%
ECO100081	ECO100081	100%	100%	100%
ECO100081	HIN101103	59%	100%	100%
ECO100081	KPN301855	93%	78.9%	100%
ECO100081	LPN102025	43%	100%	100%
ECO100081	LMO101121	36%	96.7%	96.5%
ECO100081	MAV103918	32%	94.1%	99.3%
ECO100081	MBV101485	31%	94.1%	99.3%
ECO100081	MLP100560	32%	94.1%	99.3%
ECO100081	MTU202132	31%	94.1%	99.3%
ECO100081	MGE100226	27%	98.0%	90.3%
ECO100081	MPN100522	28%	98.7%	99.3%



Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100081	NGO100621	40%	91.4%	93.4%
ECO100081	NME201917	40%	91.4%	93.4%
ECO100081	PMU100133	55%	100%	100%
ECO100081	PRT102634	77%	100%	100%
ECO100081	PAE204419	51%	100%	100%
ECO100081	PPU105962	50%	100%	100%
ECO100081	PSY103859	52%	100%	100%
ECO100081	SPA102750	93%	100%	100%
ECO100081	STY103147	93%	100%	100%
ECO100081	STM102859	94%	100%	100%
ECO100081	SAU801178	33%	98.0%	97.9%
ECO100081	SEP200891	32%	98.0%	97.9%
ECO100081	SHA101307	33%	98.0%	97.9%
ECO100081	TPA100379	34%	99.3%	96.6%
ECO100081	UUR100388	25%	96.7%	96.6%
ECO100081	YPS000986	84%	100%	100%
ECO100093	ABA100624	24%	88.0%	82.7%
ECO100093	BAN113055	20%	68.1%	70.9%
ECO100093	BAN105429	21%	68.1%	74.2%
ECO100093	BPT102987	28%	89.1%	94.5%
ECO100093	BCE102722	30%	75%	82%
ECO100093	BFU100406	28%	81.9%	88%
ECO100093	BMA104087	29%	75%	82%
ECO100093	CDP101255	29%	22.8%	31.2%
ECO100093	EBC101799	85%	100%	100%
ECO100093	ECO100093	100%	100%	100%
ECO100093	HIN101115	39%	83.7%	86.6%
ECO100093	KPN301845	88%	100%	100%
ECO100093	LPN103526	29%	85.1%	95.0%
ECO100093	MCA100437	24%	66.3%	74.6%
ECO100093	MAV103267	23%	43.8%	55.3%
ECO100093	MLP100571	24%	34.4%	27.9%
ECO100093	NGO100580	34%	85.9%	94.6%
ECO100093	NME201903	34%	85.9%	94.6%
ECO100093	PMU100145	37%	87.0%	93.4%
ECO100093	PRT102631	61%	93.8%	97.7%
ECO100093	PAE204407	31%	74.6%	70.0%
ECO100093	PPU105995	32%	90.9%	87.2%
ECO100093	PSY103839	33%	83.7%	81.3%
ECO100093	SPA101845	93%	100%	100%
ECO100093	STY103179	93%	100%	100%
ECO100093	STM102891	93%	100%	100%
ECO100093	SEP200899	22%	62.7%	39.8%
ECO100093	SHA100844	23%	62.0%	47.2%
ECO100093	VCH102364	39%	88.0%	90.4%
ECO100093	YPS001020	66%	97.5%	99.6%
ECO100094	ABA100623	30%	96.7%	95.7%
ECO100094	BAN111291	31%	94.3%	89.7%
ECO100094	BAN101900	32%	93.6%	88.2%
ECO100094	BFR102146	24%	79.8%	68.3%
ECO100094	BPT102984	45%	97.4%	98.0%
ECO100094	BBU100299	35%	98.6%	99.3%
ECO100094	BCE109663	46%	98.6%	98.8%
ECO100094	BFU100407	46%	98.6%	98.8%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100094	BMA104126	47%	98.6%	98.8%
ECO100094	CJU100645	27%	89.8%	80.3%
ECO100094	CAC100288	26%	89.0%	86.6%
ECO100094	CBO102974	28%	89.0%	85.0%
ECO100094	EBC101798	98%	100%	100%
ECO100094	EFA202170	33%	90.5%	83.6%
ECO100094	EFM201888	32%	89.8%	82.8%
ECO100094	ECO100094	100%	100%	100%
ECO100094	HIN101116	52%	100%	100%
ECO100094	HPY100962	25%	92.9%	83.9%
ECO100094	KPN300531	96%	58.3%	100%
ECO100094	LPN103001	44%	100%	100%
ECO100094	LMO101001	32%	95%	89.7%
ECO100094	MCA100438	25%	82.4%	78.9%
ECO100094	NGO100578	41%	97.6%	98.1%
ECO100094	NME201902	42%	97.1%	97.6%
ECO100094	PMU100146	50%	100%	100%
ECO100094	PRT102629	89%	100%	100%
ECO100094	PAE204406	51%	93.6%	92.6%
ECO100094	PPU111774	52%	90%	90.0%
ECO100094	PSY103837	52%	91.7%	92.2%
ECO100094	SPA101844	97%	100%	100%
ECO100094	STY103209	99%	100%	100%
ECO100094	STM102892	99%	100%	100%
ECO100094	SAU801185	24%	88.8%	76.6%
ECO100094	SEP200915	25%	88.8%	77.6%
ECO100094	SHA100845	25%	83.6%	71.9%
ECO100094	SMU100084	31%	89.0%	79.9%
ECO100094	SPN401510	33%	83.3%	74.8%
ECO100094	SPY201171	31%	89.0%	79.7%
ECO100094	TPA100385	33%	93.3%	95.9%
ECO100094	VCH102363	68%	100%	100%
ECO100094	YPS001022	95%	100%	100%
ECO100095	ABA100622	49%	95.8%	93.9%
ECO100095	BAN103024	47%	96.9%	96.4%
ECO100095	BAN112439	48%	96.9%	96.4%
ECO100095	BFR12421	43%	84.1%	74.1%
ECO100095	BPT102981	53%	97.1%	96.4%
ECO100095	BBU100298	47%	97.1%	92.3%
ECO100095	BCE103310	58%	75.7%	100%
ECO100095	BFU100408	52%	98.2%	97.7%
ECO100095	BMA104500	52%	99.7%	99.5%
ECO100095	CJU100646	40%	100%	98.9%
ECO100095	CAC100838	50%	96.9%	95.7%
ECO100095	CBO103263	49%	96.9%	96.5%
ECO100095	CDF102447	48%	98.4%	96.2%
ECO100095	CDP101254	51%	84.6%	77.9%
ECO100095	EBC101797	97%	41.5%	97.5%
ECO100095	EFA202168	51%	90.1%	84.1%
ECO100095	EFM200220	54%	82.0%	75.8%
ECO100095	ECO100095	100%	100%	100%
ECO100095	HIN101117	63%	79.9%	77.9%
ECO100095	HPY100963	40%	79.4%	79.5%
ECO100095	KPN300530	98%	41.8%	100%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100095	LPN100473	71%	9.4%	100%
ECO100095	LMO101235	46%	96.9%	96.2%
ECO100095	MCA101528	55%	85.9%	91.9%
ECO100095	MAV103265	47%	96.6%	97.7%
ECO100095	MBV100533	53%	79.4%	79.9%
ECO100095	MLP100572	45%	96.6%	97.9%
ECO100095	MTU202116	53%	79.4%	79.9%
ECO100095	MGE100229	34%	54.6%	55.6%
ECO100095	MPN100519	32%	54.0%	53.4%
ECO100095	NGO100577	48%	96.9%	95.2%
ECO100095	NME201901	48%	96.9%	95.2%
ECO100095	PMU100147	62%	87.5%	82.7%
ECO100095	PRT102627	94%	48.8%	100%
ECO100095	PAE204405	57%	100%	100%
ECO100095	PPU105993	58%	100%	100%
ECO100095	PSY103835	57%	100%	100%
ECO100095	SPA100031	91%	67.1%	98.1%
ECO100095	STY103211	98%	100%	100%
ECO100095	STM102893	98%	100%	100%
ECO100095	SAU801186	52%	81.2%	79.0%
ECO100095	SEP200917	45%	97.4%	95.2%
ECO100095	SHA100846	45%	97.4%	95.2%
ECO100095	SMU100085	51%	89.6%	78.1%
ECO100095	SPN401509	56%	80.7%	73.5%
ECO100095	SPY201170	54%	82.0%	71.3%
ECO100095	TPA100386	49%	79.4%	72.7%
ECO100095	VCH102362	75%	100%	100%
ECO100095	YPS001023	94%	100%	100%
ECO100096	ABA100621	49%	71.5%	100%
ECO100096	BFR100706	38%	88.5%	63.3%
ECO100096	BPT102979	52%	97.7%	98.0%
ECO100096	BCE106802	54%	97.4%	97.0%
ECO100096	BFU106497	53%	97.4%	97.0%
ECO100096	BMA100406	55%	97.4%	97.0%
ECO100096	CJU100121	42%	94.1%	95.9%
ECO100096	CPN200093	36%	89.2%	95.8%
ECO100096	CTR200809	38%	90.8%	95.5%
ECO100096	EBC100070	97%	37.4%	100%
ECO100096	EFA204185	36%	16.4%	7.8%
ECO100096	ECO100096	100%	100%	100%
ECO100096	HIN101118	77%	99.7%	99.7%
ECO100096	HPY101035	42%	95.4%	96.9%
ECO100096	KPN300609	94%	76.7%	100%
ECO100096	MCA100416	54%	97.0%	97.7%
ECO100096	NGO101976	48%	96.4%	96.4%
ECO100096	NME200247	49%	96.4%	96.4%
ECO100096	PMU100148	77%	99.7%	99.7%
ECO100096	PRT100138	86%	90.8%	100%
ECO100096	PAE204404	57%	99.7%	100%
ECO100096	PPU111772	56%	99.7%	100%
ECO100096	PSY103834	56%	99.7%	100%
ECO100096	SPA100700	87%	100%	100%
ECO100096	STY103212	98%	100%	100%
ECO100096	STM102894	98%	100%	100%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100096	VCH102361	73%	100%	100%
ECO100096	YPS001024	92%	100%	98.1%
ECO100102	BPT102719	31%	100%	99.2%
ECO100102	BCE111292	30%	91.5%	91.2%
ECO100102	BFU101371	31%	98.4%	98.8%
ECO100102	BMA106052	30%	98.4%	98.8%
ECO100102	EBC103445	80%	100%	100%
ECO100102	ECO100102	100%	100%	100%
ECO100102	KPN301732	76%	97.6%	100%
ECO100102	LPN101018	24%	93.9%	92.7%
ECO100102	PRT104002	53%	98.4%	97.2%
ECO100102	PPU100250	45%	16.2%	97.6%
ECO100102	SPA101560	89%	100%	100%
ECO100102	STY103218	89%	100%	100%
ECO100102	VCH102393	40%	97.6%	97.6%
ECO100102	YPS000901	67%	100%	98.8%
ECO100113	BAN100380	31%	84.6%	98.2%
ECO100113	BMA109038	39%	90.6%	63.6%
ECO100113	CDF100440	28%	89.0%	86.6%
ECO100113	EBC103453	92%	100%	100%
ECO100113	ECO100113	100%	100%	100%
ECO100113	KPN307947	90%	24.0%	92.4%
ECO100113	KPN301741	93%	100%	98.1%
ECO100113	LMO100648	28%	89.4%	95.2%
ECO100113	MAV105850	25%	90.6%	92%
ECO100113	MAV106443	25%	91.7%	94.7%
ECO100113	MAV106442	28%	86.6%	85%
ECO100113	NGO100599	34%	96.9%	94.6%
ECO100113	NME201814	34%	96.9%	94.2%
ECO100113	PRT106136	79%	98.8%	96.2%
ECO100113	PAE204765	47%	97.6%	97.7%
ECO100113	PPU100113	46%	97.6%	98.8%
ECO100113	SPA100332	95%	100%	100%
ECO100113	STY103289	96%	100%	100%
ECO100113	STM102972	96%	100%	100%
ECO100113	VCH102380	65%	98.8%	98.0%
ECO100113	YPS000871	86%	99.6%	99.6%
ECO100115	ABA105536	46%	33.7%	68.0%
ECO100115	BAN101075	31%	0.2%	45.1%
ECO100115	BAN101226	36%	17.1%	43.7%
ECO100115	BPT100902	56%	0.2%	43.0%
ECO100115	BCE106716	56%	21.1%	4.3%
ECO100115	BFU100111	53%	25.9%	13.8%
ECO100115	BMA108930	53%	20.8%	55.4%
ECO100115	CJU100863	21%	4.3%	34.7%
ECO100115	CDP100400	34%	98.7%	98.2%
ECO100115	EBC102752	90%	100%	100%
ECO100115	EFA202405	34%	37.1%	59.6%
ECO100115	BFM201990	32%	37.1%	60.1%
ECO100115	ECO100115	100%	100%	100%
ECO100115	HIN101204	68%	34.6%	58.6%
ECO100115	KPN301446	91%	100%	100%
ECO100115	LPN100774	45%	10.3%	53.9%
ECO100115	LMO102367	35%	37.1%	60.1%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100115	MCA101150	39%	19.0%	44.2%
ECO100115	MAV103601	31%	1.6%	33.2%
ECO100115	MTU405582	32%	50.2%	84.6%
ECO100115	MTU400129	32%	64.4%	99.8%
ECO100115	MGE100278	25%	16.5%	26.3%
ECO100115	MPN100447	27%	3.2%	46.0%
ECO100115	NGO100078	53%	15.6%	38.0%
ECO100115	NME201414	56%	33.2%	19.6%
ECO100115	PMU100894	72%	100%	100%
ECO100115	PRT102280	78%	100%	100%
ECO100115	PAE205011	54%	83.0%	99.3%
ECO100115	PPU105100	54%	18.7%	59.2%
ECO100115	PSY103646	52%	20.2%	43.8%
ECO100115	SPA100283	80%	60.5%	100%
ECO100115	STY103294	93%	100%	100%
ECO100115	STM102974	93%	100%	100%
ECO100115	SAU101783	36%	39.8%	77.6%
ECO100115	SPY200777	30%	3.8%	35.4%
ECO100115	VCH102378	74%	100%	99.1%
ECO100115	YPS000863	79%	14.0%	37.7%
ECO100116	ABA101766	38%	95.6%	96.4%
ECO100116	BAN101609	33%	96.4%	97.0%
ECO100116	BAN103383	44%	96.4%	97.0%
ECO100116	BFR10034	33%	94.1%	98.2%
ECO100116	BFR11786	32%	94.1%	98.7%
ECO100116	BPT100905	63%	99.6%	79.2%
ECO100116	BCE110691	66%	97.9%	79.7%
ECO100116	BFU100082	65%	99.4%	92.9%
ECO100116	BMA107694	65%	99.6%	80.0%
ECO100116	CPN201018	35%	93.0%	94.1%
ECO100116	CTR200835	38%	93.0%	94.0%
ECO100116	CBO103777	35%	93.5%	95.2%
ECO100116	CBO103904	37%	94.7%	97.0%
ECO100116	CDF102926	38%	94.7%	95.7%
ECO100116	CDP100695	36%	96.6%	98.7%
ECO100116	EBC102751	97%	100%	100%
ECO100116	EFA202404	43%	96.4%	97.4%
ECO100116	EFM201020	42%	96.4%	97.4%
ECO100116	ECO100116	100%	100%	100%
ECO100116	HIN101203	81%	100%	99.2%
ECO100116	KPN301447	96%	100%	99.8%
ECO100116	LPN100879	62%	100%	100%
ECO100116	LMO101821	43%	95.4%	96.4%
ECO100116	MCA101643	37%	98.1%	98.8%
ECO100116	MAV101768	37%	95.6%	97.0%
ECO100116	MBV103409	37%	97.0%	98.7%
ECO100116	MLP101416	34%	97.0%	98.7%
ECO100116	MTU200460	37%	97.0%	98.7%
ECO100116	MGE100277	32%	93.7%	96.3%
ECO100116	MPN100448	33%	93.7%	96.3%
ECO100116	NGO100074	63%	99.4%	81.1%
ECO100116	NME201415	63%	99.4%	81.1%
ECO100116	PMU100893	88%	100%	100%
ECO100116	PRT102281	90%	100%	99.8%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100116	PAE201586	42%	98.5%	99.4%
ECO100116	PPU103115	40%	98.5%	99.4%
ECO100116	PSY104859	41%	98.5%	99.4%
ECO100116	SPA100336	96%	83.5%	100%
ECO100116	STY103295	98%	100%	99.8%
ECO100116	STM103004	98%	100%	100%
ECO100116	SAU801096	44%	95.6%	96.4%
ECO100116	SEP200806	45%	95.6%	96.4%
ECO100116	SHA100679	44%	95.6%	96.8%
ECO100116	SMU101480	36%	93.2%	74.7%
ECO100116	SPN401048	38%	93.2%	76.5%
ECO100116	SPY200778	35%	97.5%	77.7%
ECO100116	VCH102377	89%	100%	99.8%
ECO100116	YPS000861	93%	100%	99.8%
ECO100117	BPT103682	29%	59.3%	100%
ECO100117	BCE104746	29%	31.9%	62.8%
ECO100117	BFU101391	43%	46.8%	46.8%
ECO100117	BFU100907	41%	49.3%	57.2%
ECO100117	EBC102750	48%	89.5%	100%
ECO100117	EFA200061	22%	25.8%	20.0%
ECO100117	EFA201265	22%	25.8%	20.0%
ECO100117	ECO100117	100%	100%	100%
ECO100117	KPN305987	52%	91.2%	96.4%
ECO100117	MCA102218	28%	10.9%	46.5%
ECO100117	PPU101283	36%	77.3%	91.2%
ECO100117	SPA101490	56%	88.8%	100%
ECO100117	STY103296	58%	87.8%	98.0%
ECO100117	SAU800401	27%	13.1%	11.6%
ECO100117	SPN401793	29%	14.1%	22.7%
ECO100118	ABA100442	74%	99.3%	98.7%
ECO100118	BPT102269	72%	99.1%	99.5%
ECO100118	BCE109527	73%	99.3%	99.8%
ECO100118	BFU107948	74%	99.3%	98.1%
ECO100118	CJU100774	60%	98.4%	99.2%
ECO100118	EBC106332	96%	82.5%	100%
ECO100118	ECO100118	100%	100%	100%
ECO100118	HPY100766	61%	98.4%	99.2%
ECO100118	KPN300389	95%	18.2%	90.2%
ECO100118	KPN300864	96%	93.5%	100%
ECO100118	MCA101955	73%	95.5%	99.3%
ECO100118	NGO101334	74%	99.3%	99.8%
ECO100118	NME201620	74%	99.3%	99.8%
ECO100118	PMU100204	81%	99.9%	99.5%
ECO100118	PRT101310	88%	100%	100%
ECO100118	PAE201786	79%	99.0%	98.8%
ECO100118	PPU111285	79%	96.3%	96.0%
ECO100118	PSY101607	78%	99.0%	96.3%
ECO100118	SPA100508	94%	60%	100%
ECO100118	STY103298	96%	100%	100%
ECO100118	STM103008	96%	100%	100%
ECO100118	TPA100176	31%	13.3%	37.0%
ECO100118	VCH100593	82%	99.7%	99.7%
ECO100118	YPS000857	90%	100%	100%
ECO100135	ECO100135	100%	100%	100%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100135	SPA106733	29%	40.3%	97.3%
ECO100135	STY103389	32%	98.5%	97.2%
ECO100136	ECO100136	100%	100%	100%
ECO100136	SPA109709	36%	58.6%	98.2%
ECO100136	STY103420	37%	86.4%	84.8%
ECO100139	ABA100394	33%	96.0%	97.9%
ECO100139	ABA100739	36%	92.5%	97.6%
ECO100139	BFU103132	30%	68.4%	77.5%
ECO100139	BFU103304	38%	76.4%	92.9%
ECO100139	BFU103222	33%	94.7%	87.3%
ECO100139	ECO100139	100%	100%	100%
ECO100139	KPN302863	35%	94.3%	96.5%
ECO100139	PRT105280	35%	93.9%	93.8%
ECO100139	PAE204081	35%	93.2%	94.2%
ECO100139	SPA104033	45%	96.4%	100%
ECO100139	STY103424	60%	98.3%	98.4%
ECO100139	SHA101318	19%	16.4%	31.5%
ECO100139	SPY100688	22%	23.1%	53.9%
ECO100139	TPA100432	23%	19.5%	46.1%
ECO100139	YPS000524	36%	93.1%	91.7%
ECO100140	ABA100736	35%	95.1%	96.7%
ECO100140	ABA100392	40%	88.2%	88.2%
ECO100140	BPT101284	41%	87.0%	75.9%
ECO100140	BFU103245	39%	94.7%	97.9%
ECO100140	BFU103302	47%	93.9%	93.5%
ECO100140	ECO100140	100%	100%	100%
ECO100140	KPN302865	39%	91.5%	93.6%
ECO100140	PRT105676	42%	95.9%	90.7%
ECO100140	PAE204082	39%	87.0%	85.1%
ECO100140	PPU101843	34%	43.9%	81.8%
ECO100140	PSY105016	36%	87.0%	76.6%
ECO100140	SPA104034	48%	97.2%	95.2%
ECO100140	STY103425	57%	100%	100%
ECO100140	YPS000522	41%	96.7%	92.3%
ECO100142	ABA105477	47%	88.1%	85.6%
ECO100142	BAN112513	43%	84.3%	77.8%
ECO100142	BFR100366	39%	84.9%	88.9%
ECO100142	BPT101655	40%	88.7%	85.3%
ECO100142	BCE102263	49%	49.7%	62.9%
ECO100142	BFU102640	37%	99.4%	85.7%
ECO100142	BMA109305	39%	95.0%	87.4%
ECO100142	CJU100058	29%	79.9%	80.3%
ECO100142	CAC103001	38%	84.9%	48.7%
ECO100142	CBO100107	41%	87.4%	90.7%
ECO100142	CDF102980	37%	86.2%	50.6%
ECO100142	CDP100654	36%	93.7%	90.6%
ECO100142	EBC102063	85%	88.1%	100%
ECO100142	ECO100142	100%	100%	100%
ECO100142	HIN100063	56%	99.4%	98.1%
ECO100142	HPY101019	31%	86.2%	83.4%
ECO100142	KPN308497	77%	100%	100%
ECO100142	LPN102612	37%	88.1%	98.6%
ECO100142	LMO102140	42%	84.9%	84.3%
ECO100142	MCA100865	38%	99.4%	98.8%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100142	MAV104005	38%	88.7%	78.0%
ECO100142	MBV102400	33%	84.3%	73.9%
ECO100142	MLP100158	35%	80.5%	70.2%
ECO100142	MTU203554	33%	84.3%	73.9%
ECO100142	NGO101986	42%	84.3%	81.1%
ECO100142	NME200881	43%	84.3%	81.1%
ECO100142	PMU100865	57%	92.5%	88.5%
ECO100142	PRT102518	62%	97.5%	95.2%
ECO100142	PAE204724	51%	96.9%	94.4%
ECO100142	PPU108440	48%	99.4%	99.4%
ECO100142	PSY105158	53%	96.9%	93.3%
ECO100142	SPA104025	80%	98.1%	100%
ECO100142	STY103427	89%	90.6%	90.6%
ECO100142	SAU800516	40%	89.9%	89.9%
ECO100142	SEP201849	43%	87.4%	86.8%
ECO100142	SHA100112	41%	87.4%	86.8%
ECO100142	SMU100995	42%	86.2%	77.7%
ECO100142	SPN400269	36%	97.5%	55.2%
ECO100142	SPY200833	44%	87.4%	83.1%
ECO100142	VCH100582	58%	100%	95.2%
ECO100142	YPS000787	65%	93.1%	93.1%
ECO100144	ABA104779	45%	93.8%	91.9%
ECO100144	BPT100055	48%	88.6%	96.8%
ECO100144	BCE107846	45%	88.6%	95.6%
ECO100144	BFU114519	47%	83.1%	86.6%
ECO100144	BMA109098	46%	81.8%	88.9%
ECO100144	EBC102068	78%	92.9%	90.2%
ECO100144	ECO100144	100%	100%	100%
ECO100144	KPN306084	76%	92.9%	97.6%
ECO100144	MCA102257	34%	88.3%	93.8%
ECO100144	NGO101470	46%	91.9%	98.6%
ECO100144	NME201975	45%	91.9%	98.6%
ECO100144	PAE204720	48%	92.2%	96.9%
ECO100144	PPU108420	50%	93.8%	96.3%
ECO100144	PSY105149	44%	81.8%	96.9%
ECO100144	SPA104029	79%	80.5%	98.4%
ECO100144	STY103460	81%	96.4%	99.7%
ECO100144	VCH100584	56%	96.4%	98.0%
ECO100144	YPS000781	71%	91.2%	87.5%
ECO100145	ABA104294	63%	95.4%	81.5%
ECO100145	BAN111357	29%	69.5%	51.8%
ECO100145	BAN107715	31%	69.5%	46.5%
ECO100145	BPT100533	37%	94.7%	92.2%
ECO100145	BBU100167	29%	74.2%	92%
ECO100145	BCE102976	45%	78.8%	85.5%
ECO100145	BFU114180	43%	78.8%	84.9%
ECO100145	BMA106451	46%	78.8%	85.5%
ECO100145	CJU100114	26%	76.8%	97.5%
ECO100145	CTR200677	23%	74.2%	85.8%
ECO100145	CAC101598	27%	71.5%	58.5%
ECO100145	CBO101773	30%	63.6%	54.1%
ECO100145	CDF100661	32%	32.5%	30.1%
ECO100145	EBC102067	98%	100%	100%
ECO100145	ECO100145	100%	100%	100%



Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100145	HIN100061	75%	94.0%	97.9%
ECO100145	KPN304195	98%	100%	100%
ECO100145	LPN103126	72%	88.1%	84.2%
ECO100145	MCA101582	62%	86.1%	93.5%
ECO100145	NGO101937	45%	82.1%	89.1%
ECO100145	NME200203	45%	82.1%	89.1%
ECO100145	PMU100863	80%	94.0%	97.9%
ECO100145	PRT101562	94%	100%	100%
ECO100145	PAE204719	76%	86.8%	88.5%
ECO100145	PPU108418	68%	85.4%	83.8%
ECO100145	PSY100089	76%	74.2%	96.6%
ECO100145	SPA104031	97%	30.5%	100%
ECO100145	STY103461	98%	100%	100%
ECO100145	SAU801431	32%	31.1%	80.3%
ECO100145	SPY200759	50%	19.9%	34.7%
ECO100145	TPA100095	29%	56.3%	65%
ECO100145	VCH100585	85%	95.4%	97.3%
ECO100145	YPS000779	94%	100%	100%
ECO100148	CDP101536	34%	89.7%	99.0%
ECO100148	EBC102064	78%	69.9%	100%
ECO100148	ECO100148	100%	100%	100%
ECO100148	KPN304202	81%	98.2%	100%
ECO100148	PRT101564	55%	97.8%	99.6%
ECO100148	PAE203958	47%	97.6%	99.4%
ECO100148	PPU107649	45%	96.7%	99.5%
ECO100148	PSY108786	45%	97.6%	96.6%
ECO100148	SPA101069	75%	100%	100%
ECO100148	STY103465	84%	98.7%	100%
ECO100148	STM103140	84%	100%	100%
ECO100148	VCH100590	48%	97.9%	99.5%
ECO100148	YPS000776	65%	98.1%	98.6%
ECO100150	ABA103956	29%	98.5%	99.0%
ECO100150	BFR104161	21%	22.4%	18.2%
ECO100150	BFR100416	25%	19.0%	17.3%
ECO100150	BFR10467	21%	20.3%	20.2%
ECO100150	BFR11841	27%	16.1%	17.5%
ECO100150	BFR101776	25%	17.0%	16.1%
ECO100150	BFR103964	23%	20.5%	20.3%
ECO100150	BFR104855	31%	11.8%	13.2%
ECO100150	BFR100601	22%	44.0%	33.4%
ECO100150	BFR10065	27%	16.3%	36.7%
ECO100150	BFR103068	20%	21.4%	22.6%
ECO100150	BFR104786	21%	26.6%	24.0%
ECO100150	BFR10126	22%	86.9%	79.2%
ECO100150	BPT101854	38%	93.2%	83.9%
ECO100150	BCE111433	33%	82.6%	98.4%
ECO100150	BFU107418	24%	98.4%	96.3%
ECO100150	BMA109111	34%	95.9%	94.8%
ECO100150	EBC101242	89%	96.5%	100%
ECO100150	ECO100150	100%	100%	100%
ECO100150	HIN101435	26%	39.2%	87.2%
ECO100150	KPN304208	60%	100%	100%
ECO100150	MCA102097	23%	23.2%	19.8%
ECO100150	MBV102043	29%	9.1%	35.6%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100150	MTU202942	29%	9.1%	37.6%
ECO100150	PRT104914	33%	99.7%	98.9%
ECO100150	PAE202464	38%	91.7%	80.7%
ECO100150	PPU105337	38%	94.4%	97.9%
ECO100150	PSY101285	37%	97.3%	97.2%
ECO100150	SPA100272	91%	47.4%	100%
ECO100150	STY104553	35%	98.1%	99.3%
ECO100150	STM103144	73%	100%	100%
ECO100150	TPA100587	29%	14.1%	47.5%
ECO100150	VCH100198	32%	91.3%	90.7%
ECO100150	YPS000978	26%	96.5%	98.1%
ECO100151	BFR105362	32%	78.5%	82.5%
ECO100151	BFU102313	62%	98.1%	88.1%
ECO100151	CJU101278	38%	89.8%	94.0%
ECO100151	EFA201996	42%	87.5%	91.6%
ECO100151	ECO100151	100%	100%	100%
ECO100151	HPY100874	31%	90.9%	94.9%
ECO100151	KPN304210	92%	100%	100%
ECO100151	PRT102499	36%	89.8%	94.0%
ECO100151	PPU100161	42%	86.0%	87.6%
ECO100151	SPA100271	75%	67.5%	100%
ECO100151	STY103469	91%	100%	100%
ECO100151	STM103175	92%	100%	100%
ECO100151	SMU100116	38%	90.2%	88.4%
ECO100151	VCH100199	45%	92.1%	85.6%
ECO100151	YPS000155	79%	100%	100%
ECO100153	BAN110904	27%	94.4%	45.6%
ECO100153	BAN110932	31%	94.4%	94.7%
ECO100153	BCE113442	30%	4.2%	94.8%
ECO100153	BFU103716	31%	100%	95.5%
ECO100153	BMA103709	31%	99.5%	94.9%
ECO100153	CDP100079	29%	40.2%	95.7%
ECO100153	EBC105792	81%	1.4%	98.6%
ECO100153	ECO100153	100%	100%	100%
ECO100153	KPN304213	83%	100%	100%
ECO100153	SPA103168	82%	21.2%	98.9%
ECO100153	STY103491	90%	98.8%	95.2%
ECO100153	STM103177	90%	98.8%	95.2%
ECO100153	VCH100201	36%	97.4%	97.5%
ECO100153	YPS000152	68%	98.8%	98.2%
ECO100158	ABA104905	27%	65.0%	51.6%
ECO100158	BAN107089	25%	77.4%	65.7%
ECO100158	BFR101755	22%	61.7%	44.9%
ECO100158	BPT100813	34%	91.0%	84.2%
ECO100158	BCE101181	40%	62.8%	77.5%
ECO100158	BFU105758	34%	90.2%	83.2%
ECO100158	BMA108052	36%	94.7%	83.5%
ECO100158	CJU101523	28%	73.3%	73.1%
ECO100158	CAC103091	21%	60.2%	45.6%
ECO100158	CBO101985	29%	72.9%	64.1%
ECO100158	CDP100163	27%	64.3%	53.1%
ECO100158	EBC102140	77%	99.2%	99.2%
ECO100158	ECO100158	100%	100%	100%
ECO100158	HIN101441	22%	66.2%	56.1%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100158	HPY101538	24%	74.4%	55.8%
ECO100158	KPN308672	72%	99.6%	99.6%
ECO100158	LMO101056	29%	89.1%	81.3%
ECO100158	PRT105976	50%	95.9%	95.7%
ECO100158	PAE204042	30%	93.6%	95.1%
ECO100158	PPU104488	29%	94.4%	94.4%
ECO100158	PSY103310	25%	51.9%	44.0%
ECO100158	SPA102649	75%	76.3%	99.5%
ECO100158	STY103497	80%	100%	100%
ECO100158	SAU800609	27%	89.5%	85.4%
ECO100158	SEP200175	28%	85.3%	81.7%
ECO100158	SHA101549	26%	89.5%	83.2%
ECO100158	SPY201383	20%	74.1%	68.4%
ECO100158	VCH102346	37%	90.2%	89.1%
ECO100158	YPS000147	54%	97.0%	92.9%
ECO100161	BAN110062	37%	59.3%	71.5%
ECO100161	BAN107077	36%	78.9%	67.6%
ECO100161	BFR11675	39%	75.7%	74.7%
ECO100161	BPT102297	41%	74.3%	85.3%
ECO100161	BBU100104	34%	93.9%	92.1%
ECO100161	BCE109327	36%	95.6%	92.1%
ECO100161	BMA103894	36%	94.7%	91.5%
ECO100161	CJU101153	38%	95.1%	94.7%
ECO100161	CTR200205	40%	77.6%	75.5%
ECO100161	CBO100298	43%	57.6%	67.1%
ECO100161	EBC102486	91%	100%	100%
ECO100161	EFA202055	34%	92.2%	78.0%
ECO100161	EFM201658	36%	48.3%	95.8%
ECO100161	ECO100161	100%	100%	100%
ECO100161	HPY101002	42%	79.1%	88.9%
ECO100161	KPN304180	90%	100%	100%
ECO100161	LPN103539	41%	93.5%	95.2%
ECO100161	LMO101189	36%	60.3%	60.8%
ECO100161	MAV103189	34%	56.1%	53.4%
ECO100161	MBV100882	36%	56.1%	51.3%
ECO100161	MLP100663	35%	57.2%	51.4%
ECO100161	MTU201206	35%	56.1%	49.0%
ECO100161	PAE200765	38%	77.8%	99.6%
ECO100161	PSY102326	38%	73.4%	96.8%
ECO100161	SPA102656	90%	100%	96.5%
ECO100161	STY103840	92%	100%	100%
ECO100161	STM103213	92%	100%	100%
ECO100161	SAU801728	40%	57.6%	65.8%
ECO100161	SEP202073	41%	61.8%	73.1%
ECO100161	SHA100568	40%	59.1%	67.3%
ECO100161	SMU101421	38%	57.6%	72.6%
ECO100161	SPY201695	33%	69.8%	87.2%
ECO100161	TPA100832	34%	89.2%	88.7%
ECO100161	VCH100556	58%	100%	99.8%
ECO100161	YPS000135	75%	100%	100%
ECO100167	ABA104028	40%	94.6%	95.9%
ECO100167	BPT101104	38%	88.9%	91.7%
ECO100167	BCE102413	35%	83.9%	99.6%
ECO100167	BFU101941	36%	68.2%	99.7%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100167	BMA110028	36%	92.7%	95.5%
ECO100167	CDP101162	26%	47.1%	60.8%
ECO100167	EBC103102	90%	64.9%	99.5%
ECO100167	ECO100167	100%	100%	100%
ECO100167	HIN101684	46%	92.8%	95.6%
ECO100167	KPN306317	88%	97.2%	99.8%
ECO100167	LPN101443	37%	94.9%	98.1%
ECO100167	MCA101007	33%	95.1%	96.2%
ECO100167	MAV103401	24%	48.3%	90.3%
ECO100167	MBV102319	25%	93.8%	97.3%
ECO100167	MTU202880	25%	93.8%	97.3%
ECO100167	NGO100301	33%	92.1%	95.7%
ECO100167	NME201261	33%	92.2%	95.8%
ECO100167	PMU100460	46%	96.7%	99.3%
ECO100167	PRT104542	66%	77.3%	97.3%
ECO100167	PAE203656	42%	96.2%	96.1%
ECO100167	PPU105172	41%	93.7%	94.1%
ECO100167	PSY104380	42%	94.7%	94.8%
ECO100167	SPA100030	76%	41.9%	97.4%
ECO100167	STY103845	92%	100%	100%
ECO100167	VCH102228	53%	96.9%	98.0%
ECO100167	YPS001121	76%	98.8%	96.5%
ECO100169	ABA104000	72%	92.1%	88.8%
ECO100169	BAN100446	53%	76.8%	95.7%
ECO100169	BAN110084	53%	97.9%	98.7%
ECO100169	BFR104950	47%	97.1%	84.2%
ECO100169	BPT101108	59%	97.9%	97.2%
ECO100169	BBU100122	47%	92.5%	85.8%
ECO100169	BCE101166	55%	97.9%	98.0%
ECO100169	BFU101939	59%	92.5%	89.2%
ECO100169	BMA101604	56%	97.1%	98.8%
ECO100169	CJU101107	52%	98.8%	89.7%
ECO100169	CPN200048	43%	92.1%	79.8%
ECO100169	CTR200051	45%	88.8%	75.8%
ECO100169	CAC101756	52%	93.4%	97.0%
ECO100169	CBO103187	53%	93.4%	97.0%
ECO100169	CDF101764	54%	97.5%	99.2%
ECO100169	CDP101120	50%	93.4%	85.0%
ECO100169	EBC103098	97%	100%	100%
ECO100169	EFA200418	51%	99.2%	91.2%
ECO100169	ECO100169	100%	100%	100%
ECO100169	HIN100892	82%	100%	95.6%
ECO100169	HPY101531	47%	98.8%	90.9%
ECO100169	KPN301398	98%	95.0%	100%
ECO100169	LPN100646	57%	99.2%	94.9%
ECO100169	LMO100442	53%	99.2%	96.0%
ECO100169	MCA101251	67%	92.1%	81.9%
ECO100169	MAV106404	52%	92.9%	81.2%
ECO100169	MBV102282	52%	92.9%	78.0%
ECO100169	MLP100973	52%	92.9%	80.9%
ECO100169	MTU202852	52%	92.9%	78.0%
ECO100169	MGE100072	36%	92.1%	78.5%
ECO100169	MPN100623	39%	92.5%	76.2%
ECO100169	NGO100893	53%	99.2%	100%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100169	NME200306	52%	99.2%	100%
ECO100169	PMU101984	84%	100%	95.2%
ECO100169	PRT105507	90%	100%	100%
ECO100169	PAE203654	73%	99.6%	97.2%
ECO100169	PPU107884	70%	93.8%	92.2%
ECO100169	PSY108183	72%	93.8%	84.6%
ECO100169	SPA101195	97%	100%	100%
ECO100169	STY103848	97%	100%	100%
ECO100169	STM103561	97%	100%	100%
ECO100169	SAU801256	51%	93.4%	88.2%
ECO100169	SEP201549	52%	93.4%	85.9%
ECO100169	SHA100713	50%	70.1%	81.2%
ECO100169	SMU100628	49%	99.6%	92.0%
ECO100169	SPN402017	48%	100%	93.1%
ECO100169	SPY201599	50%	100%	94.5%
ECO100169	TPA100599	48%	94.2%	78.0%
ECO100169	UUR100024	36%	91.3%	63.3%
ECO100169	VCH102226	82%	100%	100%
ECO100169	YPS001127	93%	100%	100%
ECO100170	ABA106144	54%	98.2%	97.9%
ECO100170	BAN110110	37%	94.3%	97.2%
ECO100170	BAN103067	47%	98.9%	99.0%
ECO100170	BFR10353	32%	90.5%	97.9%
ECO100170	BPT101109	49%	98.2%	97.9%
ECO100170	BBU100121	33%	87.6%	92.8%
ECO100170	BCE107064	48%	98.2%	96.9%
ECO100170	BFU100280	49%	98.2%	96.9%
ECO100170	BMA107429	49%	98.2%	96.9%
ECO100170	CJU101106	35%	98.2%	99.4%
ECO100170	CPN200047	33%	92.6%	99.6%
ECO100170	CTR200050	35%	86.9%	91.8%
ECO100170	CAC101812	44%	98.9%	99.3%
ECO100170	CBO101301	42%	98.6%	99.0%
ECO100170	CDF101762	43%	99.3%	100%
ECO100170	CDP101115	43%	92.9%	99.6%
ECO100170	EBC103096	95%	100%	100%
ECO100170	EFA200421	41%	99.3%	99.7%
ECO100170	ECO100170	100%	100%	100%
ECO100170	HIN100893	71%	98.9%	98.6%
ECO100170	HPY101532	36%	99.3%	100%
ECO100170	KPN301399	96%	100%	100%
ECO100170	LPN100716	52%	98.2%	98.6%
ECO100170	LMO102014	45%	99.6%	100%
ECO100170	MCA101252	52%	98.2%	97.6%
ECO100170	MAV106405	40%	92.9%	99.6%
ECO100170	MBV102285	39%	92.9%	99.6%
ECO100170	MLP100972	37%	92.9%	99.6%
ECO100170	MTU202851	39%	92.9%	99.6%
ECO100170	MGE100443	39%	97.2%	98.0%
ECO100170	MPN100211	40%	97.2%	98.0%
ECO100170	NGO100890	50%	99.3%	99.6%
ECO100170	NME200305	50%	99.3%	99.6%
ECO100170	PMU101985	74%	99.3%	99.6%
ECO100170	PRT104501	74%	99.3%	100%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100170	PAE203653	57%	98.2%	97.6%
ECO100170	PPU107887	58%	98.2%	97.6%
ECO100170	PSY104373	58%	98.2%	97.6%
ECO100170	SPA101193	96%	100%	100%
ECO100170	STY103870	96%	100%	100%
ECO100170	STM103563	96%	100%	100%
ECO100170	SAU801257	43%	99.3%	100%
ECO100170	SEP201550	43%	98.2%	99.3%
ECO100170	SHA100714	43%	98.2%	99.3%
ECO100170	SMU100627	38%	98.2%	97.7%
ECO100170	SPN402016	39%	98.2%	97.7%
ECO100170	SPY201600	38%	98.2%	97.7%
ECO100170	TPA100598	30%	90.8%	95.9%
ECO100170	UUR100520	39%	97.9%	99.0%
ECO100170	VCH102225	70%	98.2%	98.9%
ECO100170	YPS001128	77%	100%	100%
ECO100171	ABA101328	60%	99.2%	100%
ECO100171	BAN107431	43%	97.5%	98.3%
ECO100171	BAN103009	48%	97.5%	98.3%
ECO100171	BFR104169	53%	90.0%	98.6%
ECO100171	BPT101110	55%	95.9%	97.1%
ECO100171	BCE109906	58%	95.9%	97.5%
ECO100171	BFU100279	57%	95.9%	97.5%
ECO100171	BMA109323	57%	95.9%	97.5%
ECO100171	CJU101199	49%	92.9%	94.1%
ECO100171	CPN200046	38%	96.3%	94.0%
ECO100171	CTR200049	38%	88.4%	88.2%
ECO100171	CAC103602	49%	96.7%	97.9%
ECO100171	CBO103420	47%	97.5%	97.9%
ECO100171	CDF101760	47%	97.1%	98.7%
ECO100171	CDP101114	44%	97.9%	96.7%
ECO100171	EBC103094	97%	100%	100%
ECO100171	EFA200424	48%	97.1%	97.9%
ECO100171	ECO100171	100%	100%	100%
ECO100171	HIN101042	77%	97.5%	99.2%
ECO100171	HPY100764	51%	93.8%	94.6%
ECO100171	KPN301400	98%	100%	100%
ECO100171	LPN101596	61%	95.9%	93.9%
ECO100171	LMO102234	47%	96.7%	97.1%
ECO100171	MCA100778	60%	98.3%	98.8%
ECO100171	MAV106392	46%	96.3%	87.2%
ECO100171	MBV102299	45%	96.3%	88.5%
ECO100171	MLP100970	46%	96.3%	82.8%
ECO100171	MTU202845	45%	96.3%	88.5%
ECO100171	MGE100444	35%	90.9%	90.5%
ECO100171	MPN100210	34%	95.0%	97.9%
ECO100171	NGO100888	53%	95.9%	96.7%
ECO100171	NME200304	53%	95.9%	96.7%
ECO100171	PMU101986	79%	98.3%	97.9%
ECO100171	PRT104887	91%	99.6%	99.2%
ECO100171	PAE203652	69%	97.9%	96.3%
ECO100171	PPU102433	69%	97.9%	95.5%
ECO100171	PSY104372	69%	96.7%	94.3%
ECO100171	SPA101722	94%	47.3%	100%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100171	STY103871	98%	100%	100%
ECO100171	STM103564	98%	100%	100%
ECO100171	SAU801258	44%	96.7%	97.5%
ECO100171	SEP201551	45%	100%	100%
ECO100171	SHA100715	45%	100%	90.9%
ECO100171	SMU101143	47%	97.5%	96.3%
ECO100171	SPN400845	49%	97.9%	96.0%
ECO100171	SPY200331	48%	97.5%	97.5%
ECO100171	TPA100098	31%	25.3%	24.3%
ECO100171	UUR100519	35%	96.3%	98.7%
ECO100171	VCH102224	85%	100%	99.2%
ECO100171	YPS001129	90%	100%	100%
ECO100179	ABA101312	39%	97.7%	99.1%
ECO100179	BFR105934	35%	97.1%	96.0%
ECO100179	BPT101128	42%	91.5%	89.3%
ECO100179	BCE111319	41%	99.1%	98.3%
ECO100179	BFU114742	39%	96.5%	92.7%
ECO100179	BMA109885	39%	97.4%	96.1%
ECO100179	CJU100537	34%	95.3%	99.7%
ECO100179	CPN200450	34%	98.5%	94.7%
ECO100179	CTR200507	33%	99.1%	96.9%
ECO100179	CBO103766	28%	23.8%	84.3%
ECO100179	EBC103091	89%	100%	100%
ECO100179	ECO100179	100%	100%	100%
ECO100179	HIN100894	65%	98.5%	99.1%
ECO100179	HPY100193	31%	90.9%	91.4%
ECO100179	KPN301403	92%	90.6%	100%
ECO100179	LPN102597	35%	99.1%	99.7%
ECO100179	MCA100324	44%	87.7%	90.8%
ECO100179	NGO100826	38%	97.7%	96.3%
ECO100179	NME200082	38%	97.7%	96.3%
ECO100179	PMU101994	65%	98.2%	98.5%
ECO100179	PRT101247	80%	100%	99.7%
ECO100179	PAE203644	51%	98.2%	94.9%
ECO100179	PPU101150	49%	98.5%	95.7%
ECO100179	PSY104345	50%	98.2%	95.4%
ECO100179	SPA100512	85%	83.6%	58.2%
ECO100179	STY103879	95%	100%	100%
ECO100179	STM103592	95%	100%	100%
ECO100179	VCH102216	64%	100%	97.2%
ECO100179	YPS001147	82%	99.7%	100%
ECO100180	ABA101324	44%	94.0%	100%
ECO100180	BAN112058	43%	56.3%	92.2%
ECO100180	BAN101529	48%	92.1%	95.1%
ECO100180	BPT101129	51%	92.1%	94.7%
ECO100180	BCE105358	58%	96.0%	94.2%
ECO100180	BFU107782	52%	96.0%	93.5%
ECO100180	BFU105730	55%	96.7%	94.8%
ECO100180	BMA107929	57%	96.0%	94.2%
ECO100180	CJU100245	47%	90.1%	94.5%
ECO100180	CPN200094	44%	92.1%	91.5%
ECO100180	CTR200808	43%	90.1%	89.5%
ECO100180	CAC102008	45%	89.4%	94.3%
ECO100180	CBO103374	45%	90.7%	93.8%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100180	CDF104046	51%	25.8%	97.5%
ECO100180	CDF101479	42%	57.6%	95.5%
ECO100180	CDF100018	52%	78.8%	96.7%
ECO100180	EBC103090	93%	39.1%	78.7%
ECO100180	EBC100020	91%	57.0%	84.3%
ECO100180	EBC100023	91%	57.0%	84.3%
ECO100180	EFA203430	50%	90.1%	95.0%
ECO100180	EFM202041	50%	90.1%	96.4%
ECO100180	ECO100180	100%	100%	100%
ECO100180	HIN101039	68%	92.7%	93.9%
ECO100180	HPY101356	46%	88.7%	86.8%
ECO100180	KPN301913	97%	100%	100%
ECO100180	LPN101746	52%	84.8%	89.0%
ECO100180	LMO100873	51%	93.4%	96.5%
ECO100180	MCA100038	44%	96.0%	83.4%
ECO100180	MBV105275	29%	45.0%	31.9%
ECO100180	NGO100839	55%	92.7%	94.0%
ECO100180	NME200083	55%	92.7%	94.0%
ECO100180	PMU101995	70%	96.7%	95.4%
ECO100180	PRT101246	83%	97.4%	85.5%
ECO100180	PAE203643	54%	94.0%	98.6%
ECO100180	PPU101164	57%	92.1%	96.6%
ECO100180	PSY104344	56%	94.0%	98.6%
ECO100180	SPA100773	99%	100%	100%
ECO100180	STY103910	99%	100%	100%
ECO100180	STM103593	98%	100%	100%
ECO100180	SAU802098	46%	89.4%	91.1%
ECO100180	SEP204192	44%	89.4%	91.7%
ECO100180	SHA100083	38%	35.8%	93.1%
ECO100180	SMU100534	46%	92.1%	97.1%
ECO100180	SPN400384	46%	92.1%	97.1%
ECO100180	SPY201345	46%	92.1%	97.8%
ECO100180	VCH102215	64%	97.4%	96.1%
ECO100180	YPS001148	89%	100%	83.4%
ECO100183	ABA101887	65%	93.4%	98.9%
ECO100183	BAN111817	53%	82.3%	68.9%
ECO100183	BAN113438	54%	90.9%	69.6%
ECO100183	BFR12457	51%	88.4%	87.6%
ECO100183	BPT101141	58%	93.4%	92.0%
ECO100183	BBU100046	37%	89.4%	98.3%
ECO100183	BCE104245	60%	94.4%	87.4%
ECO100183	BFU105066	58%	92.4%	74.2%
ECO100183	BMA107189	60%	94.4%	87.4%
ECO100183	CJU100010	38%	87.9%	88.5%
ECO100183	CPN200642	41%	96.0%	88.8%
ECO100183	CTR200293	46%	92.4%	84.3%
ECO100183	CAC100322	41%	89.4%	71.7%
ECO100183	CBO102656	41%	91.9%	69.1%
ECO100183	CDF100890	49%	88.9%	69.0%
ECO100183	CDP101132	45%	79.8%	93.6%
ECO100183	EBC102552	89%	100%	100%
ECO100183	EFA201281	50%	91.9%	71.0%
ECO100183	EFM202475	51%	91.9%	72.1%
ECO100183	ECO100183	100%	100%	100%



Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100183	HIN101036	72%	96.5%	98.0%
ECO100183	HPY101305	33%	92.9%	91.9%
ECO100183	KPN301923	89%	100%	99.5%
ECO100183	LPN101418	62%	90.9%	93.2%
ECO100183	LMO102644	47%	91.9%	69.3%
ECO100183	MCA101524	38%	90.9%	85.8%
ECO100183	MAV102888	46%	91.4%	76.6%
ECO100183	MBV102296	48%	91.4%	69.3%
ECO100183	MLP100982	48%	91.4%	75.4%
ECO100183	MTU202864	48%	91.4%	69.3%
ECO100183	NGO100782	61%	92.9%	95.4%
ECO100183	NME200070	61%	92.9%	95.4%
ECO100183	PMU101998	72%	96.5%	97.5%
ECO100183	PRT101243	75%	98.5%	99.5%
ECO100183	PAE203640	71%	94.4%	93.0%
ECO100183	PPU101167	72%	92.4%	88.4%
ECO100183	PSY106718	71%	92.4%	82.4%
ECO100183	STY103913	92%	100%	100%
ECO100183	STM103626	92%	100%	100%
ECO100183	SAU801244	44%	92.9%	71.8%
ECO100183	SEP201538	45%	91.4%	69.2%
ECO100183	SHA101009	43%	91.4%	70.6%
ECO100183	SMU100101	45%	93.4%	71.9%
ECO100183	SPN401044	49%	91.4%	69.5%
ECO100183	SPY200888	46%	90.9%	69.2%
ECO100183	UUR100400	35%	38.9%	25.3%
ECO100183	VCH102212	73%	93.9%	90.3%
ECO100183	YPS001153	84%	97.5%	97.5%
ECO100184	ABA101411	48%	99.6%	96.4%
ECO100184	BAN112326	36%	99.2%	99.5%
ECO100184	BFR102018	33%	96.8%	95.0%
ECO100184	BPT101552	48%	99.7%	99.3%
ECO100184	BBU100578	38%	99.2%	98.1%
ECO100184	BCE115231	49%	99.9%	100%
ECO100184	BFU107633	47%	99.9%	99.7%
ECO100184	BMA101634	48%	99.9%	100%
ECO100184	CJU100668	39%	89.9%	88.7%
ECO100184	CPN200079	37%	92.5%	89.8%
ECO100184	CTR200821	36%	92.5%	90.0%
ECO100184	CAC103161	39%	90.5%	91.0%
ECO100184	CBO100607	34%	99.7%	99.8%
ECO100184	CBO101196	35%	99.6%	99.2%
ECO100184	CDF101163	40%	92.2%	91.0%
ECO100184	CDP101233	34%	98.8%	99.1%
ECO100184	EBC102553	94%	100%	100%
ECO100184	EFA202115	32%	96.2%	96.7%
ECO100184	EFM200294	32%	99.1%	99.5%
ECO100184	ECO100184	100%	100%	100%
ECO100184	HIN100720	71%	99.9%	99.8%
ECO100184	HPY101439	39%	92.5%	91.3%
ECO100184	KPN301922	95%	100%	100%
ECO100184	LPN102982	56%	99.6%	99.7%
ECO100184	LMO100629	35%	99.4%	99.8%
ECO100184	MCA102321	49%	89.4%	86.7%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100184	MAV100203	34%	7.7%	90.7%
ECO100184	MAV103371	35%	99.2%	99.5%
ECO100184	MBV102577	35%	97.8%	99.1%
ECO100184	MLP100747	35%	99.2%	99.5%
ECO100184	MTU201526	36%	98.8%	98.7%
ECO100184	MGE100266	27%	72.6%	89.6%
ECO100184	MPN100459	36%	18.4%	19.4%
ECO100184	NGO101860	47%	99.9%	100%
ECO100184	NME200585	47%	99.9%	100%
ECO100184	PMU100034	71%	99.9%	99.8%
ECO100184	PRT101242	85%	98.6%	100%
ECO100184	PAE203638	58%	99.5%	99.6%
ECO100184	PPU100137	58%	99.9%	99.9%
ECO100184	PSY104339	57%	99.5%	99.6%
ECO100184	SPA100912	92%	99.3%	100%
ECO100184	STY103914	96%	100%	100%
ECO100184	STM103627	96%	100%	100%
ECO100184	SAU801703	33%	93.0%	93.8%
ECO100184	SEP201707	33%	92.0%	92.4%
ECO100184	SHA100359	33%	96.0%	94.2%
ECO100184	SMU101018	30%	90.8%	92.0%
ECO100184	SPN400795	31%	95.3%	95.0%
ECO100184	SPY200987	29%	96.2%	96.8%
ECO100184	TPA100661	39%	92.8%	90.7%
ECO100184	UUR100419	29%	87.0%	94.4%
ECO100184	VCH102211	76%	100%	99.6%
ECO100184	YPS001155	88%	100%	99.1%
ECO100185	ABA100308	57%	80.9%	94.1%
ECO100185	BAN105768	55%	97.8%	95.4%
ECO100185	BPT101398	64%	99.4%	97.8%
ECO100185	BCE106451	64%	99.4%	97.2%
ECO100185	BFU100947	64%	99.4%	97.2%
ECO100185	BMA107589	64%	99.4%	97.2%
ECO100185	CJU100411	49%	98.4%	97.8%
ECO100185	CPN200335	44%	98.7%	96.3%
ECO100185	CTR200529	45%	98.7%	96.3%
ECO100185	CAC100492	52%	81.8%	95.3%
ECO100185	CBO102220	51%	89.3%	50.3%
ECO100185	CDF101403	50%	96.6%	97.1%
ECO100185	EBC102554	96%	100%	100%
ECO100185	EFA200247	52%	79.6%	96.9%
ECO100185	EFM200190	55%	81.5%	99.6%
ECO100185	ECO100185	100%	100%	100%
ECO100185	HIN100386	74%	99.7%	99.7%
ECO100185	HPY100550	48%	98.1%	96.8%
ECO100185	KPN301921	96%	100%	100%
ECO100185	LPN101352	62%	84.0%	99.3%
ECO100185	LMO100159	52%	98.4%	97.8%
ECO100185	MCA100190	60%	80.3%	100%
ECO100185	MLP100072	28%	46.4%	27.9%
ECO100185	NGO100369	64%	98.1%	97.2%
ECO100185	NME201237	64%	98.1%	97.2%
ECO100185	PMU100292	75%	99.7%	99.7%
ECO100185	PRT100667	69%	99.7%	99.7%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100185	PRT101241	88%	99.7%	99.7%
ECO100185	PAE203637	69%	99.4%	99.4%
ECO100185	PPU101171	67%	99.4%	99.7%
ECO100185	PSY108491	67%	99.4%	99.1%
ECO100185	SPA100816	80%	88.4%	100%
ECO100185	STY103916	97%	100%	100%
ECO100185	STM103628	97%	100%	100%
ECO100185	SAU801700	52%	97.8%	98.4%
ECO100185	SEP201704	52%	97.8%	98.4%
ECO100185	SHA100923	52%	97.8%	98.1%
ECO100185	SMU100529	54%	79.9%	98.0%
ECO100185	SPN400387	50%	79.9%	98.4%
ECO100185	SPY201342	52%	79.9%	98.0%
ECO100185	VCH102210	75%	99.7%	99.7%
ECO100185	YPS001157	90%	99.7%	99.7%
ECO100193	CJU100189	40%	16.1%	23.4%
ECO100193	ECO100193	100%	100%	100%
ECO100193	KPN300059	73%	55.8%	100%
ECO100193	KPN301914	66%	88.7%	92.5%
ECO100193	TPA100217	26%	29.1%	82.4%
ECO100193	YPS000139	43%	83.6%	84.2%
ECO100194	ABA100529	68%	99.3%	100%
ECO100194	BAN100354	47%	99.0%	99.3%
ECO100194	BAN103931	51%	99.8%	100%
ECO100194	BFR100495	28%	33.2%	0.2%
ECO100194	BPT102439	60%	96.7%	96.5%
ECO100194	BBU100401	28%	87.1%	65.4%
ECO100194	BCE111561	67%	38.6%	99.5%
ECO100194	BFU106495	56%	99.8%	99.1%
ECO100194	BMA104091	56%	99.8%	99.1%
ECO100194	CJU100505	45%	99.7%	99.6%
ECO100194	CPN200251	43%	97.4%	97.5%
ECO100194	CTR200662	39%	99.7%	97.9%
ECO100194	CAC100467	49%	98.4%	97.4%
ECO100194	CBO100123	28%	98.6%	98.3%
ECO100194	CDF100404	47%	12.8%	76.6%
ECO100194	CDF100250	47%	98.6%	97.5%
ECO100194	CDP100483	40%	99.5%	99.1%
ECO100194	EBC102546	93%	99.8%	100%
ECO100194	EFA200454	47%	96.7%	95.8%
ECO100194	EFM201684	47%	99.0%	98.6%
ECO100194	ECO100194	100%	100%	100%
ECO100194	HIN100709	75%	99.7%	99.5%
ECO100194	HPY100234	39%	99.8%	99.7%
ECO100194	KPN301911	94%	96.0%	100%
ECO100194	LPN102483	71%	16.4%	100%
ECO100194	LMO100624	49%	99.0%	98.8%
ECO100194	MCA101839	60%	98.4%	99.5%
ECO100194	MAV102826	40%	97.4%	97.6%
ECO100194	MBV103229	40%	97.4%	97.6%
ECO100194	MLP100951	27%	93.0%	73.1%
ECO100194	MTU202807	40%	97.7%	97.3%
ECO100194	NGO100106	60%	98.4%	98.4%
ECO100194	NME201412	60%	98.4%	98.4%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100194	PMU101370	76%	99.0%	98.9%
ECO100194	PRT101177	79%	99.7%	99.8%
ECO100194	PAE200955	71%	99.7%	99.6%
ECO100194	PPU108855	68%	96.5%	99.6%
ECO100194	PSY105509	67%	99.8%	99.8%
ECO100194	SPA100809	89%	98.4%	100%
ECO100194	STY103990	95%	100%	100%
ECO100194	SAU801263	44%	99.5%	99.1%
ECO100194	SEP201556	46%	99.8%	99.5%
ECO100194	SHA101150	47%	98.3%	97.9%
ECO100194	SMU101082	40%	99.0%	99.2%
ECO100194	SPN400243	42%	99.0%	99.0%
ECO100194	SPY201510	41%	99.0%	98.9%
ECO100194	TPA100158	40%	93.7%	93.7%
ECO100194	VCH100859	71%	99.0%	99.1%
ECO100194	YPS002005	84%	99.8%	99.8%
ECO100195	ABA103785	37%	94.5%	93.0%
ECO100195	BAN110343	34%	40%	58.0%
ECO100195	CBO101676	39%	39.6%	91.4%
ECO100195	CDF101307	33%	43.8%	65.2%
ECO100195	EBC102547	82%	100%	100%
ECO100195	ECO100195	100%	100%	100%
ECO100195	HIN100489	51%	94.5%	92.9%
ECO100195	KPN301908	85%	100%	100%
ECO100195	MCA100700	39%	74.9%	93.7%
ECO100195	NGO100030	42%	98.7%	98.2%
ECO100195	NME200229	42%	96.2%	95.6%
ECO100195	PMU101170	54%	93.6%	89.4%
ECO100195	PRT101178	62%	100%	100%
ECO100195	PAE203386	48%	90.2%	89.6%
ECO100195	PPU108086	47%	90.2%	90%
ECO100195	PSY104415	45%	95.3%	95.2%
ECO100195	SPA100206	89%	37.9%	100%
ECO100195	STY103991	88%	100%	100%
ECO100195	VCH100860	52%	98.3%	99.1%
ECO100195	YPS002007	71%	100%	100%
ECO100197	ABA101419	34%	88.6%	99.2%
ECO100197	ABA101431	41%	81.9%	81.2%
ECO100197	BAN110744	44%	91.5%	96.2%
ECO100197	BAN101917	44%	94.5%	96.3%
ECO100197	BPT102034	47%	100%	100%
ECO100197	BCE106577	56%	87.1%	80.3%
ECO100197	BFU102067	50%	96.3%	95.9%
ECO100197	BMA104983	54%	97.0%	96.3%
ECO100197	CJU100709	37%	85.6%	89.9%
ECO100197	CJU101125	41%	80.4%	81.3%
ECO100197	CJU100710	42%	84.9%	87.9%
ECO100197	CJU100711	45%	82.3%	86.0%
ECO100197	CPN200473	31%	93.0%	93.8%
ECO100197	CAC100740	40%	95.2%	93.4%
ECO100197	CBO102481	33%	92.3%	92.6%
ECO100197	CBO101824	41%	94.5%	94.1%
ECO100197	CBO103909	45%	91.9%	92.2%
ECO100197	CDF100529	43%	97.8%	98.5%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100197	CDP100114	31%	98.2%	91.7%
ECO100197	CDP100115	32%	94.5%	88.3%
ECO100197	EBC102539	96%	100%	100%
ECO100197	EFA201785	40%	98.2%	97.5%
ECO100197	EFM201963	38%	98.2%	97.2%
ECO100197	ECO100197	100%	100%	100%
ECO100197	HIN100600	60%	98.9%	99.6%
ECO100197	HPY101541	42%	97.4%	97.8%
ECO100197	KPN301905	95%	100%	100%
ECO100197	LPN100686	45%	95.2%	98.8%
ECO100197	LMO100978	47%	94.5%	93.8%
ECO100197	MCA103679	55%	98.5%	99.3%
ECO100197	NGO101326	37%	96.3%	94.1%
ECO100197	NME200471	38%	96.3%	94.1%
ECO100197	PMU101730	58%	98.9%	99.6%
ECO100197	PRT100159	78%	100%	100%
ECO100197	PAE205500	47%	78.6%	81.2%
ECO100197	PPU101952	47%	78.6%	82.4%
ECO100197	PSY101363	51%	78.6%	82.1%
ECO100197	SPA101556	37%	88.2%	87.3%
ECO100197	STY103993	96%	100%	100%
ECO100197	STM100616	37%	88.2%	87.3%
ECO100197	SAU800839	36%	97.0%	98.2%
ECO100197	SEP201451	37%	97.0%	98.1%
ECO100197	SHA100334	38%	92.6%	93.0%
ECO100197	SHA101832	35%	97.0%	97.4%
ECO100197	SMU100488	33%	93.4%	93.6%
ECO100197	SPN400147	35%	96.7%	97.5%
ECO100197	SPY200233	36%	100%	100%
ECO100197	TPA100812	34%	98.9%	98.5%
ECO100197	VCH100889	68%	100%	97.8%
ECO100197	YPS002011	90%	100%	100%
ECO100198	ABA101423	45%	100%	99.1%
ECO100198	BAN105551	52%	76.0%	81.3%
ECO100198	BAN106583	47%	96.3%	94.6%
ECO100198	BPT103178	52%	100%	100%
ECO100198	BCE112661	54%	98.2%	100%
ECO100198	BFU102065	54%	100%	95.2%
ECO100198	BMA106456	54%	98.2%	100%
ECO100198	CJU100712	44%	89.4%	64.0%
ECO100198	CPN200472	36%	95.9%	94.1%
ECO100198	CAC101527	43%	96.3%	95.9%
ECO100198	CBO103376	48%	95.9%	98.6%
ECO100198	CDF100530	48%	92.6%	92.2%
ECO100198	CDP100111	39%	94.5%	91.1%
ECO100198	EBC102541	97%	100%	100%
ECO100198	EFA201706	46%	93.5%	89.0%
ECO100198	EFM202483	44%	94.9%	91.2%
ECO100198	ECO100198	100%	100%	100%
ECO100198	HPY101554	43%	96.3%	96.7%
ECO100198	KPN301904	95%	100%	100%
ECO100198	LPN101477	53%	99.1%	99.1%
ECO100198	LMO100259	45%	98.2%	95.5%
ECO100198	MCA103062	45%	98.6%	93.9%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100198	NGO101323	43%	96.3%	91.7%
ECO100198	NME200470	43%	96.3%	91.7%
ECO100198	PMU101729	49%	95.4%	90.8%
ECO100198	PRT100130	83%	100%	100%
ECO100198	PAE202349	48%	98.6%	98.6%
ECO100198	PPU109980	50%	97.7%	100%
ECO100198	PSY103687	48%	98.2%	94.7%
ECO100198	SPA100613	90%	85.3%	100%
ECO100198	STY103994	92%	97.7%	100%
ECO100198	STM100618	44%	93.5%	92.7%
ECO100198	SAU800463	50%	95.9%	95.0%
ECO100198	SEP201771	50%	95.9%	95.0%
ECO100198	SHA100333	46%	98.6%	89.0%
ECO100198	SMU100477	40%	97.2%	90.8%
ECO100198	SPN400150	41%	94.5%	88.7%
ECO100198	SPY200235	42%	94.5%	92.7%
ECO100198	TPA100118	40%	95.4%	95.0%
ECO100198	VCH100890	53%	96.8%	93.3%
ECO100198	YPS002016	90%	100%	100%
ECO100201	ABA104598	65%	100%	100%
ECO100201	BPT102715	65%	100%	100%
ECO100201	BCE100085	66%	99.3%	93.6%
ECO100201	EBC100779	90%	85.4%	97.9%
ECO100201	ECO100201	100%	100%	100%
ECO100201	KPN301057	90%	100%	100%
ECO100201	PRT104732	81%	100%	100%
ECO100201	PAE204164	65%	99.3%	97.4%
ECO100201	PPU111521	67%	100%	100%
ECO100201	SPA101642	90%	100%	100%
ECO100201	STY104030	91%	100%	100%
ECO100201	STM103710	92%	100%	100%
ECO100201	YPS002027	75%	100%	100%
ECO100223	BAN108547	31%	33.0%	38.5%
ECO100223	BAN105487	31%	44.4%	80%
ECO100223	ECO100223	100%	100%	100%
ECO100223	VCH100877	26%	64.8%	54.4%
ECO100223	YPS002852	49%	94.3%	84.2%
ECO100236	ABA101495	43%	99.5%	97.9%
ECO100236	BAN105079	42%	96.2%	95.7%
ECO100236	BAN100068	43%	98.6%	98.1%
ECO100236	BFR101900	41%	97.1%	96.9%
ECO100236	BPT102346	44%	99.8%	98.3%
ECO100236	BCE107136	45%	98.3%	89.0%
ECO100236	BMA109567	45%	98.3%	89.7%
ECO100236	CJU100520	38%	97.6%	97.8%
ECO100236	CAC102032	47%	97.8%	96.7%
ECO100236	CDP101216	45%	96.2%	93.5%
ECO100236	EBC103210	88%	100%	100%
ECO100236	EFA200208	46%	99.8%	99.3%
ECO100236	EFM200382	46%	99.5%	99.0%
ECO100236	ECO100236	100%	100%	100%
ECO100236	HIN101211	62%	99.8%	99.8%
ECO100236	KPN302476	86%	100%	100%
ECO100236	LPN100519	40%	98.1%	97.4%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100236	LMO101153	46%	99.5%	99.0%
ECO100236	MAV103439	48%	96.9%	90.1%
ECO100236	MBV104414	47%	96.6%	93.3%
ECO100236	MLP100899	45%	97.8%	96.8%
ECO100236	MTU202391	47%	96.6%	93.3%
ECO100236	NGO101136	44%	97.8%	97.4%
ECO100236	NME201166	45%	97.8%	97.4%
ECO100236	PMU100936	65%	99.8%	99.0%
ECO100236	PRT105196	71%	99.8%	99.8%
ECO100236	PAE204004	48%	99.5%	97.9%
ECO100236	PPU112135	43%	96.2%	98.5%
ECO100236	PSY105063	45%	99.5%	97.4%
ECO100236	SPA104265	83%	100%	100%
ECO100236	STY104449	86%	100%	100%
ECO100236	STM103861	86%	100%	100%
ECO100236	SMU101435	48%	99.8%	99.3%
ECO100236	SPN400833	46%	97.4%	97.1%
ECO100236	SPY201284	47%	99.5%	99.0%
ECO100236	TPA100346	44%	97.6%	97.9%
ECO100236	VCH102239	58%	99.8%	99.3%
ECO100236	YPS002651	72%	100%	99.5%
ECO100239	BFU102395	50%	89.2%	65.3%
ECO100239	EBC103227	98%	63.9%	100%
ECO100239	ECO102590	81%	90.5%	89.4%
ECO100239	ECO101961	81%	93.7%	100%
ECO100239	ECO100239	100%	100%	100%
ECO100239	LPN103162	46%	66.5%	95.5%
ECO100239	SEP200678	37%	43.7%	65.7%
ECO100240	EBC103228	85%	100%	72.0%
ECO100240	ECO100240	100%	100%	100%
ECO100240	KPN202940	29%	86.8%	94.4%
ECO100240	KPN204064	29%	87.5%	95.7%
ECO100240	KPN200664	29%	86.8%	94.4%
ECO100240	PRT102844	43%	73.7%	100%
ECO100245	EBC103236	92%	99.7%	100%
ECO100245	ECO100245	100%	100%	100%
ECO100245	NME200125	22%	84.0%	81.8%
ECO100255	ABA104682	35%	80.8%	32.0%
ECO100255	ECO100255	100%	100%	100%
ECO100255	HIN100123	69%	83.3%	28.0%
ECO100255	PMU100956	75%	85.8%	25.5%
ECO100255	PRT102521	90%	85.8%	26.2%
ECO100255	VCH103408	81%	85.8%	25%
ECO100256	EBC101194	98%	31.7%	100%
ECO100256	EBC101311	92%	47.3%	98.8%
ECO100256	EBC103715	88%	58.1%	100%
ECO100256	EBC103943	90%	74.9%	100%
ECO100256	EBC104524	90%	74.9%	100%
ECO100256	EBC103604	99%	100%	100%
ECO100256	ECO100266	100%	100%	100%
ECO100256	ECO100256	100%	100%	100%
ECO100256	KPN302635	99%	100%	100%
ECO100256	KPN301602	99%	100%	100%
ECO100256	KPN303307	99%	100%	100%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100256	KPN306562	99%	100%	100%
ECO100256	KPN308721	99%	100%	100%
ECO100256	KPN302324	99%	100%	100%
ECO100256	KPN301774	99%	100%	100%
ECO100256	KPN301257	97%	47.9%	100%
ECO100256	KPN300832	91%	56.3%	100%
ECO100256	KPN302225	100%	65.9%	100%
ECO100256	KPN300593	96%	98.8%	100%
ECO100256	KPN302471	99%	100%	100%
ECO100256	KPN300357	99%	100%	100%
ECO100256	KPN300875	99%	100%	100%
ECO100256	STY100327	99%	100%	100%
ECO100256	STY104877	99%	100%	100%
ECO100256	STY104954	99%	100%	100%
ECO100257	EBC103602	100%	100%	100%
ECO100257	ECO100257	100%	100%	100%
ECO100257	ECO100267	100%	100%	100%
ECO100257	KPN302325	100%	100%	100%
ECO100257	KPN308692	100%	100%	100%
ECO100257	KPN306262	100%	100%	100%
ECO100257	KPN301718	98%	58.2%	89.8%
ECO100257	KPN301773	100%	82.4%	90.4%
ECO100257	KPN305294	95%	100%	100%
ECO100257	KPN302468	100%	100%	100%
ECO100257	KPN300876	100%	100%	100%
ECO100257	KPN301600	100%	100%	100%
ECO100257	KPN303306	100%	100%	100%
ECO100257	KPN302228	100%	100%	100%
ECO100257	NGO100079	32%	81.3%	38.4%
ECO100257	STY100087	100%	100%	100%
ECO100257	STY105122	100%	100%	100%
ECO100257	STY104783	100%	100%	100%
ECO100262	BFR11395	35%	96.3%	98.5%
ECO100262	EBC102936	98%	100%	100%
ECO100262	ECO100262	100%	100%	100%
ECO100262	SPN401706	27%	21.1%	25.4%
ECO100298	BAN105357	48%	100%	100%
ECO100298	BAN100434	51%	100%	99.6%
ECO100298	BFR102281	32%	100%	99.6%
ECO100298	BCE100671	35%	99.6%	91.3%
ECO100298	BFU114123	36%	98.7%	98.3%
ECO100298	BMA102603	37%	98.7%	98.3%
ECO100298	CJU100066	33%	99.2%	95.9%
ECO100298	CDP101095	42%	99.6%	92.7%
ECO100298	EFA201476	44%	98.7%	92.9%
ECO100298	ECO100298	100%	100%	100%
ECO100298	HPY100137	36%	100%	98.8%
ECO100298	NGO101247	35%	99.6%	91.5%
ECO100298	NME201508	35%	99.6%	91.5%
ECO100298	PMU101853	73%	100%	100%
ECO100298	PRT100774	72%	100%	100%
ECO100298	PRT101849	78%	99.6%	97.1%
ECO100315	BCE100919	27%	28.8%	31.5%
ECO100315	EBC101762	85%	99.4%	98.7%



Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100315	ECO100315	100%	100%	100%
ECO100350	ECO100350	100%	100%	100%
ECO100361	ABA100700	46%	97.0%	95.2%
ECO100361	BAN101055	43%	93.7%	97.5%
ECO100361	BAN100517	51%	93.1%	95.1%
ECO100361	BPT100922	45%	93.7%	94.7%
ECO100361	BCE101370	45%	93.7%	96.4%
ECO100361	BFU101599	44%	94.9%	97.0%
ECO100361	BMA104829	46%	93.7%	96.4%
ECO100361	CJU100923	51%	94.3%	98.2%
ECO100361	CPN200001	45%	92.8%	94.6%
ECO100361	CTR200001	43%	93.4%	94.9%
ECO100361	CAC102676	49%	94.3%	99.1%
ECO100361	CBO101832	48%	93.4%	96.9%
ECO100361	CDF102168	49%	94.6%	98.5%
ECO100361	CDP100775	49%	94.9%	98.8%
ECO100361	EBC102698	93%	66.9%	100%
ECO100361	ECO100361	100%	100%	100%
ECO100361	HPY100160	51%	94.0%	98.1%
ECO100361	KPN308372	91%	96.7%	100%
ECO100361	LPN101016	50%	93.4%	95.2%
ECO100361	LMO100837	51%	95.2%	98.8%
ECO100361	MCA101135	46%	93.1%	95.2%
ECO100361	MAV107884	48%	93.4%	97.2%
ECO100361	MBV102362	47%	93.4%	96.9%
ECO100361	MLP101436	46%	93.1%	96.0%
ECO100361	MTU200510	47%	93.4%	96.4%
ECO100361	NGO100861	43%	93.4%	94.1%
ECO100361	NME200933	44%	93.4%	94.1%
ECO100361	PMU101692	41%	93.7%	94.1%
ECO100361	PRT102370	77%	95.2%	98.2%
ECO100361	PAE205238	40%	93.7%	94.7%
ECO100361	PPUI10651	76%	94.3%	97.5%
ECO100361	PSY101277	42%	94.0%	95.2%
ECO100361	SPA101546	90%	85.4%	99.6%
ECO100361	STY104591	93%	96.7%	100%
ECO100361	SAU801668	49%	92.8%	96.9%
ECO100361	SEP201642	49%	92.8%	96.9%
ECO100361	SHA101765	42%	58.5%	98.0%
ECO100361	VCH100105	44%	93.7%	92.2%
ECO100361	YPS000599	43%	93.7%	94.1%
ECO100362	ECO100362	100%	100%	100%
ECO100366	BFR101178	24%	34.9%	57.0%
ECO100366	CJU100896	19%	55.0%	36.6%
ECO100366	CDP102949	27%	21.6%	9.1%
ECO100366	EBC102756	70%	96.6%	100%
ECO100366	ECO100366	100%	100%	100%
ECO100366	LPN101403	23%	25.9%	39.1%
ECO100366	PRT103239	21%	51.8%	36.1%
ECO100366	SPA101548	89%	70.7%	100%
ECO100366	STY104592	89%	97.0%	47.2%
ECO100366	STM104306	91%	100%	47.8%
ECO100367	EBC102015	28%	77.0%	100%
ECO100367	EBC102758	51%	91.0%	97.6%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100367	ECO100367	100%	100%	100%
ECO100367	KPN304631	34%	78.8%	100%
ECO100367	SPA101549	68%	98.6%	100%
ECO100367	STY104593	71%	93.2%	100%
ECO100367	STM104307	71%	93.2%	100%
ECO100381	EBC102823	83%	96.8%	96.8%
ECO100381	ECO100381	100%	100%	100%
ECO100381	KPN304881	79%	98.4%	98.4%
ECO100381	STY100328	95%	98.4%	98.4%
ECO100381	STM104352	93%	98.4%	98.4%
ECO100390	ABA100709	34%	73.5%	72.5%
ECO100390	BAN111886	25%	64.5%	73.0%
ECO100390	BAN113193	23%	98.5%	97.9%
ECO100390	BFR11820	28%	96%	99.2%
ECO100390	BPT100403	35%	21.2%	23.5%
ECO100390	BBU100828	26%	82.8%	82.6%
ECO100390	BCE105254	23%	22.8%	24.4%
ECO100390	BFU106002	34%	21.5%	23.4%
ECO100390	CAC100402	26%	84%	85.3%
ECO100390	CBO100412	26%	92.2%	92.2%
ECO100390	CDF103755	25%	89.5%	92.6%
ECO100390	CDP101084	24%	62%	58.7%
ECO100390	EBC101912	81%	99.8%	98.3%
ECO100390	EFA200864	26%	97.2%	97.9%
ECO100390	EFM200128	24%	96%	99.5%
ECO100390	ECO100390	100%	100%	100%
ECO100390	KPN308651	78%	99.8%	99.5%
ECO100390	LMO102080	27%	96.8%	97.6%
ECO100390	MCA101153	32%	95.8%	90.7%
ECO100390	MAV100736	24%	62%	58.2%
ECO100390	MLP100687	27%	21.2%	23.0%
ECO100390	MTU406882	27%	21.2%	30.2%
ECO100390	PRT101271	55%	96.8%	96.3%
ECO100390	PAE204279	31%	92%	91.4%
ECO100390	PPU105701	33%	92%	92.2%
ECO100390	PSY101474	31%	99.8%	99.5%
ECO100390	SPA101178	81%	100%	98.3%
ECO100390	STY100355	83%	100%	100%
ECO100390	SAU801345	23%	97.8%	98.9%
ECO100390	SEP202011	21%	97.8%	98.9%
ECO100390	SHA100866	23%	72.2%	73.8%
ECO100390	SPN201925	26%	16%	16.3%
ECO100390	TPA100619	26%	63.2%	62.9%
ECO100390	VCH103245	28%	72.8%	74.4%
ECO100390	YPS002608	60%	98.8%	96.9%
ECO100394	ABA104913	59%	99.6%	97.2%
ECO100394	BAN112358	49%	94.7%	95.8%
ECO100394	BAN100163	52%	98.2%	97.6%
ECO100394	BCE101232	61%	94.7%	100%
ECO100394	BMA101593	62%	95.2%	96.0%
ECO100394	EBC101456	91%	54.9%	100%
ECO100394	EFA201477	33%	98.7%	98%
ECO100394	ECO100394	100%	100%	100%
ECO100394	KPN304910	93%	100%	100%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100394	MPN100528	22%	71.8%	65.7%
ECO100394	PRT102253	60%	96.9%	97.6%
ECO100394	PAE205092	63%	95.6%	94.2%
ECO100394	PPU106756	60%	93.2%	95.3%
ECO100394	PSY101310	63%	96.9%	97.2%
ECO100394	SPA101112	94%	98.0%	99.6%
ECO100394	STY100389	95%	99.6%	99.8%
ECO100394	STM100031	95%	99.6%	99.8%
ECO100394	YPS002596	81%	98.7%	97.4%
ECO100395	BAN101050	31%	73.1%	70.0%
ECO100395	BAN109230	33%	73.1%	69.8%
ECO100395	BFR12473	26%	64.0%	70.0%
ECO100395	CAC100478	27%	64.1%	82.9%
ECO100395	CDF104139	31%	74.4%	71.2%
ECO100395	EBC101457	84%	79.0%	100%
ECO100395	EFA202423	30%	68.6%	65.8%
ECO100395	EFM200019	29%	82.5%	82.5%
ECO100395	ECO100395	100%	100%	100%
ECO100395	KPN304911	79%	99.5%	99.5%
ECO100395	LMO100614	31%	73.2%	70.7%
ECO100395	SPA105253	92%	4.5%	90%
ECO100395	SPA101113	81%	44.1%	100%
ECO100395	STY100390	83%	99.8%	99.8%
ECO100395	STM100032	83%	99.8%	99.8%
ECO100395	SPN400948	29%	72.9%	70.0%
ECO100395	SPY201005	32%	75.0%	73.0%
ECO100395	YPS002575	57%	99.5%	99.0%
ECO100402	BAN107351	47%	26.1%	35.6%
ECO100402	BFR102271	29%	60.9%	24.5%
ECO100402	EBC103463	93%	100%	100%
ECO100402	ECO100402	100%	100%	100%
ECO100402	KPN301340	90%	100%	97.5%
ECO100402	PRT101447	89%	100%	100%
ECO100402	PPU108585	56%	88.7%	79.7%
ECO100402	PSY105486	56%	88.7%	79.0%
ECO100402	SPA103227	96%	100%	100%
ECO100402	STY100420	96%	100%	100%
ECO100402	STM100071	96%	100%	100%
ECO100402	YPS000205	82%	98.3%	100%
ECO100404	EBC101277	64%	58.8%	100%
ECO100404	ECO100404	100%	100%	100%
ECO100404	KPN303448	70%	88.4%	97.8%
ECO100404	SPA103216	73%	89.9%	100%
ECO100404	STY100423	74%	89.9%	100%
ECO100407	ABA103638	62%	91.7%	91.0%
ECO100407	BAN110020	44%	96.2%	100%
ECO100407	BAN104354	54%	96.2%	97.4%
ECO100407	BFR104554	42%	88.5%	83.5%
ECO100407	BPT100012	39%	94.9%	85.5%
ECO100407	BCE102848	40%	96.2%	84.8%
ECO100407	BFU108808	42%	96.8%	86.9%
ECO100407	BMA102272	41%	93.6%	81.5%
ECO100407	CJU100351	50%	98.7%	100%
ECO100407	CPN200977	27%	98.7%	100%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100407	CTR200105	37%	99.4%	98.7%
ECO100407	CAC100789	52%	98.7%	98.7%
ECO100407	CBO101079	57%	98.7%	99.4%
ECO100407	CDF101258	55%	97.4%	95.6%
ECO100407	CDP100290	42%	94.2%	92.3%
ECO100407	EBC101280	98%	100%	100%
ECO100407	ECO100407	100%	100%	100%
ECO100407	HIN101269	76%	100%	90.2%
ECO100407	HPY100002	50%	99.4%	99.4%
ECO100407	KPN308524	100%	100%	87.2%
ECO100407	LPN100108	43%	90.4%	90.3%
ECO100407	MCA103693	60%	90.4%	85.4%
ECO100407	MAV100814	44%	91.7%	85.9%
ECO100407	MBV102145	44%	91.7%	87.5%
ECO100407	MLP100346	42%	90.4%	88.8%
ECO100407	MTU201397	44%	91.7%	90.9%
ECO100407	NGO100984	45%	96.8%	94.3%
ECO100407	NME200821	44%	96.8%	94.3%
ECO100407	PMU100731	73%	100%	99.4%
ECO100407	PRT100213	83%	99.4%	99.4%
ECO100407	PAE204050	56%	100%	98.1%
ECO100407	PPU104481	57%	100%	98.1%
ECO100407	PSY108754	52%	100%	98.1%
ECO100407	SPA108738	90%	100%	90.2%
ECO100407	STY100427	91%	100%	100%
ECO100407	STM100098	91%	100%	100%
ECO100407	SAU801767	58%	82.7%	96.2%
ECO100407	SEP202131	56%	96.2%	97.4%
ECO100407	SHA101039	58%	94.9%	96.7%
ECO100407	SPN400161	54%	100%	100%
ECO100407	VCH102234	65%	98.7%	89.0%
ECO100407	YPS002509	86%	99.4%	99.4%
ECO100408	ABA101072	44%	97.8%	91.3%
ECO100408	BAN105057	32%	87.8%	93.1%
ECO100408	BAN110216	35%	87.8%	93.1%
ECO100408	BFR105998	27%	62.6%	28.6%
ECO100408	BPT100014	45%	95.0%	88.3%
ECO100408	BBU100107	33%	85.6%	86.2%
ECO100408	BCE111817	43%	97.8%	93.8%
ECO100408	BFU113008	42%	97.1%	93.8%
ECO100408	BMA102557	44%	97.8%	93.8%
ECO100408	CJU100350	34%	89.9%	93.9%
ECO100408	CPN200850	23%	91.4%	78.5%
ECO100408	CTR200214	25%	90.6%	79.3%
ECO100408	CAC103566	31%	87.8%	91.1%
ECO100408	CBO100362	33%	89.2%	97.2%
ECO100408	CDF101805	31%	66.9%	55.6%
ECO100408	CDP100352	32%	91.4%	66.8%
ECO100408	EBC101281	93%	100%	100%
ECO100408	EFA202204	34%	87.8%	81.5%
ECO100408	EFM100580	31%	90.6%	91.3%
ECO100408	ECO100408	100%	100%	100%
ECO100408	HIN101270	54%	95.7%	92.4%
ECO100408	HPY100001	30%	89.9%	90.6%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100408	KPN308025	94%	100%	100%
ECO100408	LPN101606	40%	93.5%	88.4%
ECO100408	LMO102626	37%	91.4%	96.1%
ECO100408	MCA103036	34%	94.2%	82.3%
ECO100408	MAV101907	36%	87.8%	80.8%
ECO100408	MBV101339	34%	87.8%	43.4%
ECO100408	MLP100320	35%	89.2%	67.4%
ECO100408	MTU202496	34%	87.8%	80.8%
ECO100408	NGO100982	42%	96.4%	95.0%
ECO100408	NME200820	42%	96.4%	95.0%
ECO100408	PMU100730	63%	95.7%	92.4%
ECO100408	PRT103311	74%	74.8%	100%
ECO100408	PAE204049	55%	96.4%	84.3%
ECO100408	PPU111159	53%	96.4%	80.7%
ECO100408	PSY102195	51%	96.4%	81.2%
ECO100408	SPA103662	94%	40.3%	100%
ECO100408	STY100428	96%	100%	100%
ECO100408	STM100099	96%	100%	100%
ECO100408	SAU801524	34%	88.5%	95.3%
ECO100408	SEP200894	35%	88.5%	95.3%
ECO100408	SHA100990	34%	88.5%	96.1%
ECO100408	SMU101206	31%	89.9%	90.2%
ECO100408	SPN400390	34%	89.9%	87.0%
ECO100408	SPY201398	30%	89.9%	88%
ECO100408	TPA101005	35%	90.6%	91.5%
ECO100408	UUR100302	28%	54.0%	59.8%
ECO100408	VCH102233	53%	97.1%	95.5%
ECO100408	YPS002505	84%	99.3%	100%
ECO100409	ABA105144	46%	98.2%	99.3%
ECO100409	BFR11172	30%	97.5%	95.9%
ECO100409	BPT100016	43%	98.2%	93.8%
ECO100409	BCE110120	53%	52%	85%
ECO100409	BFU102731	49%	97.8%	97.3%
ECO100409	BMA107273	44%	96.9%	99.1%
ECO100409	CJU101376	27%	82.5%	88.6%
ECO100409	CDP100279	31%	74.8%	72.3%
ECO100409	EBC101282	84%	99.4%	100%
ECO100409	ECO100409	100%	100%	100%
ECO100409	HIN101271	52%	99.1%	93.9%
ECO100409	KPN303432	84%	99.4%	100%
ECO100409	LPN101227	52%	82.2%	83.3%
ECO100409	MCA103652	39%	91.7%	99.7%
ECO100409	MAV101439	35%	82.8%	82.4%
ECO100409	MBV102049	36%	82.8%	81.4%
ECO100409	MLP101022	35%	81.8%	82.5%
ECO100409	MTU202939	36%	82.8%	81.4%
ECO100409	NGO100695	42%	97.8%	99.1%
ECO100409	NME201944	43%	97.8%	99.1%
ECO100409	PMU100729	53%	99.1%	99.7%
ECO100409	PRT100038	67%	99.1%	98.8%
ECO100409	PAE204048	45%	98.8%	98.8%
ECO100409	PPU104483	45%	98.2%	98.1%
ECO100409	PSY102181	47%	99.1%	99.4%
ECO100409	SPA103660	87%	100%	100%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100409	STY100439	87%	100%	100%
ECO100409	STM100100	88%	100%	100%
ECO100409	VCH102232	54%	99.1%	96.1%
ECO100409	YPS002502	75%	99.7%	98.5%
ECO100424	ABA103655	43%	93.7%	96.9%
ECO100424	BAN111570	28%	72.4%	88.2%
ECO100424	BAN110867	33%	85.1%	92.4%
ECO100424	BPT102774	55%	85.7%	88.8%
ECO100424	BCE104834	59%	78.1%	93.5%
ECO100424	BFU101934	57%	83.2%	93.5%
ECO100424	BMA107732	57%	88.6%	92.6%
ECO100424	BMA109512	56%	89.5%	97.2%
ECO100424	CDP100360	28%	24.8%	21.0%
ECO100424	EBC101217	95%	100%	100%
ECO100424	ECO100424	100%	100%	100%
ECO100424	KPN303418	85%	47.9%	100%
ECO100424	LMO100640	34%	94.0%	81.0%
ECO100424	MAV102952	26%	39.0%	37.5%
ECO100424	MBV101465	22%	42.9%	27.2%
ECO100424	MTU202140	22%	42.9%	25%
ECO100424	PRT103954	67%	98.4%	98.4%
ECO100424	PAE201316	57%	95.2%	90.0%
ECO100424	PPU101498	57%	97.5%	99.7%
ECO100424	PSY104255	56%	96.5%	96.5%
ECO100424	SPA102308	76%	100%	100%
ECO100424	STY100721	95%	100%	99.1%
ECO100424	SAU801061	35%	81.0%	68.0%
ECO100424	SEP200354	38%	81.0%	66.6%
ECO100424	SHA100551	40%	58.4%	59.5%
ECO100424	YPS001897	66%	96.5%	99.7%
ECO100430	ABA101466	71%	93.6%	91.3%
ECO100430	BAN100418	59%	22.6%	96.9%
ECO100430	BAN109620	38%	94.3%	97.8%
ECO100430	BAN107278	65%	68.2%	93.4%
ECO100430	BAN111361	61%	96.5%	96.4%
ECO100430	BFR100135	54%	86.1%	94.8%
ECO100430	BPT100486	71%	100%	93.2%
ECO100430	BBU100611	53%	96.7%	95.8%
ECO100430	BCE114986	74%	97.4%	97.6%
ECO100430	BFU100995	73%	97.4%	97.6%
ECO100430	BMA101609	73%	97.4%	97.6%
ECO100430	CJU100247	55%	94.6%	96.2%
ECO100430	CPN201004	57%	96.0%	98.3%
ECO100430	CTR200078	57%	96.0%	98.3%
ECO100430	CAC101555	61%	96.9%	94.7%
ECO100430	CBO100837	62%	97.4%	93.7%
ECO100430	CDF102979	61%	96.5%	97.8%
ECO100430	CDP101237	61%	96.2%	96.7%
ECO100430	EBC101545	95%	98.3%	100%
ECO100430	EFA202273	60%	95.5%	96.6%
ECO100430	EFM101238	60%	96.5%	97.6%
ECO100430	ECO100430	100%	100%	100%
ECO100430	HIN100694	69%	97.4%	100%
ECO100430	HPY101354	51%	94.3%	97.1%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100430	KPN301083	98%	100%	100%
ECO100430	LMO102362	62%	96.2%	96.2%
ECO100430	MCA101655	65%	93.4%	97.0%
ECO100430	MAV102304	62%	96.0%	96.0%
ECO100430	MBV101048	61%	96.9%	96.9%
ECO100430	MLP100910	61%	96.2%	96.2%
ECO100430	MTU202421	61%	96.9%	96.9%
ECO100430	NGO101085	69%	94.1%	97.8%
ECO100430	NME201444	69%	94.1%	97.8%
ECO100430	PMU101977	73%	94.6%	98.1%
ECO100430	PRT101501	88%	100%	100%
ECO100430	PAE201801	77%	98.3%	97.9%
ECO100430	PPU109917	77%	98.8%	98.4%
ECO100430	PSY107890	77%	98.3%	97.9%
ECO100430	SPA102998	97%	98.8%	99.8%
ECO100430	STY100725	97%	100%	100%
ECO100430	STM100438	98%	100%	100%
ECO100430	SAU801674	61%	94.1%	94.0%
ECO100430	SEP201649	61%	94.1%	94.0%
ECO100430	SHA100379	56%	44.8%	92.5%
ECO100430	SMU100958	59%	94.1%	96.6%
ECO100430	SPN401426	58%	96.7%	98.8%
ECO100430	SPY200660	59%	94.1%	96.8%
ECO100430	TPA100504	56%	93.6%	95.4%
ECO100430	VCH101891	84%	100%	100%
ECO100430	YPS001881	92%	100%	100%
ECO100431	ABA100033	61%	24.2%	90.3%
ECO100431	ABA105304	55%	97.6%	95.2%
ECO100431	BAN104528	44%	96.9%	99.6%
ECO100431	BAN103992	53%	97.7%	96.3%
ECO100431	BFR11925	45%	97.4%	94.3%
ECO100431	BPT100489	68%	98.2%	95.5%
ECO100431	BBU100612	39%	97.7%	97.3%
ECO100431	BCE108504	69%	98.2%	95.3%
ECO100431	BFU100993	70%	98.5%	95.5%
ECO100431	BMA107557	69%	99.4%	96.6%
ECO100431	CJU100999	39%	97.1%	98.4%
ECO100431	CPN200737	40%	97.8%	95.1%
ECO100431	CTR200613	40%	97.1%	94.6%
ECO100431	CAC100342	47%	97.1%	98.1%
ECO100431	CBO101096	50%	98.0%	99.6%
ECO100431	CDF102998	52%	97.2%	97.3%
ECO100431	EBC101544	98%	54.5%	100%
ECO100431	ECO100431	100%	100%	100%
ECO100431	HIN100442	74%	98.3%	96.3%
ECO100431	HPY101359	39%	97.1%	98.9%
ECO100431	KPN301084	96%	62.6%	100%
ECO100431	MCA100771	52%	98.9%	96.8%
ECO100431	MAV107390	50%	47.6%	95.6%
ECO100431	MLP100403	40%	8.2%	19.4%
ECO100431	MGE100244	41%	96.2%	98.2%
ECO100431	MPN100504	40%	96.2%	98.2%
ECO100431	NGO100249	65%	98.1%	95.5%
ECO100431	NME201277	65%	98.9%	97.0%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100431	PMU101978	75%	99.4%	96.8%
ECO100431	PRT101500	88%	100%	100%
ECO100431	PAE201802	70%	97.8%	96.0%
ECO100431	PPU106533	70%	97.8%	96.0%
ECO100431	PSY103927	69%	97.8%	96.0%
ECO100431	SPA102997	99%	100%	98.4%
ECO100431	STY100726	99%	100%	100%
ECO100431	STM100439	99%	100%	100%
ECO100431	SPN401780	25%	15.9%	41.4%
ECO100431	SPY101613	24%	13.8%	42.9%
ECO100431	TPA100519	43%	98.3%	87.7%
ECO100431	UUR100350	40%	96.7%	99.0%
ECO100431	VCH101890	82%	100%	99.6%
ECO100431	YPS001875	91%	100%	100%
ECO100435	ABA106138	24%	96.2%	84.2%
ECO100435	BFR102134	27%	79.5%	78.4%
ECO100435	BFU104105	26%	95.5%	83.9%
ECO100435	CAC102936	39%	55.3%	54.1%
ECO100435	EBC102273	87%	99.2%	99.2%
ECO100435	ECO100435	100%	100%	100%
ECO100435	KPN302385	85%	98.5%	97.7%
ECO100435	LPN102857	30%	85.6%	83.1%
ECO100435	MCA100454	24%	78.8%	64.6%
ECO100435	MAV107513	22%	97.0%	94.2%
ECO100435	MBV101527	26%	96.2%	92.8%
ECO100435	MTU202439	26%	96.2%	92.8%
ECO100435	NGO101290	40%	96.2%	97.6%
ECO100435	NME200457	40%	96.2%	97.6%
ECO100435	PRT106164	55%	97.0%	94.8%
ECO100435	SPA102993	93%	100%	100%
ECO100435	STY100750	94%	100%	100%
ECO100435	STM100443	94%	100%	100%
ECO100435	SPN401264	26%	75.8%	33.1%
ECO100435	TPA100154	37%	90.2%	88.8%
ECO100435	YPS001867	69%	99.2%	97.0%
ECO100445	BAN103966	24%	61.1%	4.8%
ECO100445	BAN105784	24%	61.1%	43.0%
ECO100445	BMA103371	31%	43.7%	23.7%
ECO100445	CJU101094	30%	44.2%	93.3%
ECO100445	EBC101949	75%	81.6%	98.1%
ECO100445	ECO100445	100%	100%	100%
ECO100445	KPN302393	70%	84.2%	98.8%
ECO100445	MAV100663	25%	55.3%	53.0%
ECO100445	PAE203672	38%	54.2%	77.3%
ECO100445	PPU105141	40%	52.1%	74.2%
ECO100445	PSY107733	35%	53.2%	98.1%
ECO100445	SPA103161	84%	100%	100%
ECO100445	STY100781	88%	100%	100%
ECO100445	STM100473	88%	100%	100%
ECO100445	VCH101045	43%	47.9%	63.6%
ECO100445	YPS001806	55%	87.4%	94.2%
ECO100448	ECO100448	100%	100%	100%
ECO100448	KPN302401	62%	48.5%	100%
ECO100448	PAE202198	27%	94.8%	95.1%



Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100448	PPU101997	30%	97.1%	93.8%
ECO100448	SPA103158	77%	49.2%	100%
ECO100448	STY100783	67%	99.2%	99.6%
ECO100453	ABA101792	57%	99.1%	99.3%
ECO100453	BPT100257	67%	98.8%	97.6%
ECO100453	BCE114545	66%	24.5%	84.0%
ECO100453	BCE104032	66%	99.5%	98.6%
ECO100453	BFU105569	65%	100%	98.2%
ECO100453	BMA106830	66%	99.9%	98.2%
ECO100453	EBC103991	92%	100%	100%
ECO100453	ECO100453	100%	100%	100%
ECO100453	HIN100875	32%	97.9%	97.4%
ECO100453	KPN303893	91%	100%	100%
ECO100453	LPN101626	40%	98.9%	99.4%
ECO100453	MCA100461	56%	99.9%	99.7%
ECO100453	MAV103904	24%	18.5%	20.4%
ECO100453	MBV105073	23%	19.9%	19.1%
ECO100453	MTU201501	23%	19.5%	16.7%
ECO100453	NGO100607	48%	99.9%	98.7%
ECO100453	NME201818	49%	99.9%	98.7%
ECO100453	PMU101132	31%	97.6%	97.1%
ECO100453	PRT104879	75%	99.3%	99.2%
ECO100453	PAE200425	70%	98.5%	98.6%
ECO100453	PPU101135	65%	99.0%	98.7%
ECO100453	PSY103933	65%	99.3%	99.5%
ECO100453	STY100789	94%	99.9%	99.9%
ECO100453	YPS001789	84%	99.8%	99.6%
ECO100456	BCE114237	32%	23.7%	57.2%
ECO100456	BFU101219	28%	27.1%	67.2%
ECO100456	CPN200570	19%	22.7%	58.7%
ECO100456	CTR100201	19%	37.5%	48.0%
ECO100456	CDP102443	27%	12.8%	29.9%
ECO100456	EBC103983	84%	97.2%	99.9%
ECO100456	ECO100456	100%	100%	100%
ECO100456	HIN100185	35%	97.2%	98.4%
ECO100456	KPN300148	83%	14.6%	100%
ECO100456	KPN303886	83%	99.7%	97.9%
ECO100456	LPN100506	21%	82.6%	90.8%
ECO100456	MLP100103	19%	19.0%	26.4%
ECO100456	MPN100367	22%	38.7%	9.5%
ECO100456	PMU100358	38%	97.7%	98.5%
ECO100456	PRT105555	48%	97.3%	98.3%
ECO100456	PAE205017	39%	97.1%	97.0%
ECO100456	PPU102036	40%	97.4%	98.5%
ECO100456	PSY103682	41%	94.7%	93.7%
ECO100456	SPA102914	88%	95.2%	100%
ECO100456	STY100812	89%	99.8%	99.8%
ECO100456	STM100504	89%	99.7%	99.7%
ECO100456	UUR100392	24%	13.8%	11.3%
ECO100456	YPS001764	59%	97.4%	96.3%
ECO100457	EBC106191	73%	84.9%	73.8%
ECO100457	ECO100457	100%	100%	100%
ECO100457	KPN303890	75%	84.9%	78.9%
ECO100457	PRT105806	58%	94.3%	94.1%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100457	SPA102916	80%	92.5%	92.7%
ECO100457	STY100814	80%	92.5%	92.7%
ECO100457	VCH101828	58%	81.1%	61.4%
ECO100457	YPS003930	57%	84.9%	88.2%
ECO100458	CDP100984	27%	56%	24.8%
ECO100458	EBC103989	56%	100%	100%
ECO100458	ECO100458	100%	100%	100%
ECO100458	KPN300488	55%	92%	100%
ECO100458	KPN303892	59%	100%	100%
ECO100458	PMU100990	20%	97.1%	95.1%
ECO100458	PRT104644	35%	98.3%	97.2%
ECO100458	PAE108407	28%	88.6%	23.8%
ECO100458	SPA102917	72%	97.7%	100%
ECO100458	VCH101827	32%	81.1%	79.1%
ECO100458	YPS001761	36%	98.3%	97.2%
ECO100464	ABA105152	52%	99.7%	99.4%
ECO100464	BFR105086	32%	90.2%	82.4%
ECO100464	BPT101320	59%	99.2%	98.1%
ECO100464	BBU100559	41%	98.4%	93.4%
ECO100464	BCE101760	60%	99.4%	99.1%
ECO100464	BFU107645	61%	99.5%	98.9%
ECO100464	BMA108677	61%	98.7%	99.2%
ECO100464	CJU100481	43%	98.4%	98.8%
ECO100464	CAC101040	39%	98.4%	99.0%
ECO100464	CBO103036	41%	42.6%	99.6%
ECO100464	CDF102736	29%	96.0%	95.7%
ECO100464	EBC103981	91%	100%	100%
ECO100464	ECO100464	100%	100%	100%
ECO100464	HIN100103	75%	99.5%	98.7%
ECO100464	HPY100206	45%	98.6%	98.4%
ECO100464	KPN303864	91%	100%	100%
ECO100464	LPN102583	62%	99.5%	99.2%
ECO100464	LMO102556	23%	98.6%	98.2%
ECO100464	MCA100562	50%	98.6%	98.6%
ECO100464	MAV101501	48%	97.1%	96.7%
ECO100464	MBV105727	45%	98.4%	98.0%
ECO100464	MLP100990	45%	98.4%	98.0%
ECO100464	MTU202265	45%	98.4%	98.0%
ECO100464	NGO100474	25%	19.9%	34.3%
ECO100464	NME200399	25%	19.9%	18.6%
ECO100464	PMU101024	76%	99.2%	98.4%
ECO100464	PRT105522	81%	99.7%	99.0%
ECO100464	PAE201595	61%	99.4%	98.4%
ECO100464	PPU101233	60%	99.4%	98.7%
ECO100464	PSY105027	60%	99.4%	98.7%
ECO100464	SPA100495	91%	91.7%	99.7%
ECO100464	STY100841	94%	100%	98.7%
ECO100464	STM100533	94%	100%	98.7%
ECO100464	TPA100974	41%	98.4%	98.7%
ECO100464	VCH100968	69%	99.2%	98.1%
ECO100464	YPS001737	86%	100%	99.7%
ECO100465	ABA102578	62%	99.5%	99.1%
ECO100465	BAN108855	43%	100%	98.6%
ECO100465	BAN106781	47%	100%	98.6%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100465	BFR10586	39%	98.6%	96.8%
ECO100465	BPT101280	60%	99.5%	99.1%
ECO100465	BBU100416	35%	99.5%	98.1%
ECO100465	BCE114693	65%	96.3%	96.4%
ECO100465	BFU106856	65%	96.3%	96.4%
ECO100465	BMA102106	65%	96.7%	96.8%
ECO100465	CJU100600	25%	98.1%	94.3%
ECO100465	CPN200508	34%	83.6%	83.6%
ECO100465	CTR200398	32%	94.9%	83.0%
ECO100465	CAC102891	48%	100%	99.1%
ECO100465	CBO103787	51%	100%	98.6%
ECO100465	CDF102350	52%	100%	96.4%
ECO100465	CDP100003	40%	86.4%	87.3%
ECO100465	EBC103984	96%	100%	100%
ECO100465	EFA201978	45%	99.5%	98.6%
ECO100465	EFM200623	45%	99.5%	99.1%
ECO100465	ECO100465	100%	100%	100%
ECO100465	HIN100331	71%	100%	100%
ECO100465	HPY100611	30%	61.2%	72.3%
ECO100465	KPN303865	96%	100%	100%
ECO100465	LPN102084	55%	99.5%	99.1%
ECO100465	LMO102187	46%	99.5%	98.6%
ECO100465	MCA101231	61%	99.5%	98.6%
ECO100465	MAV102071	38%	100%	99.4%
ECO100465	MBV101628	37%	100%	99.4%
ECO100465	MLP101114	39%	86.4%	87.3%
ECO100465	MTU200730	37%	100%	99.4%
ECO100465	MGE100174	34%	84.6%	84.6%
ECO100465	MPN100646	32%	86.0%	86.5%
ECO100465	NGO100911	62%	100%	99.5%
ECO100465	NME200954	64%	100%	99.5%
ECO100465	PMU100284	71%	99.5%	99.5%
ECO100465	PRT104973	81%	100%	100%
ECO100465	PAE203684	64%	96.7%	96.7%
ECO100465	PPU107935	64%	96.7%	96.8%
ECO100465	PSY104919	60%	81.3%	96.2%
ECO100465	SPA100230	92%	100%	91.8%
ECO100465	STY100842	96%	100%	100%
ECO100465	STM100555	96%	100%	100%
ECO100465	SAU802229	47%	99.5%	98.6%
ECO100465	SEP200243	47%	99.5%	98.6%
ECO100465	SHA100179	47%	99.5%	98.1%
ECO100465	SMU100597	43%	85.0%	85.8%
ECO100465	SPN400210	38%	99.5%	98.1%
ECO100465	SPY200058	40%	99.5%	98.1%
ECO100465	TPA100588	38%	98.6%	97.2%
ECO100465	UUR100253	33%	99.5%	98.1%
ECO100465	VCH100969	73%	99.5%	99.5%
ECO100465	YPS001716	87%	100%	100%
ECO100468	ABA104316	27%	50.7%	63.8%
ECO100468	EBC103990	93%	100%	100%
ECO100468	ECO100468	100%	100%	100%
ECO100468	KPN303867	89%	100%	100%
ECO100468	MCA101546	24%	57.4%	72.1%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100468	PRT103854	82%	100%	100%
ECO100468	SPA107646	92%	100%	100%
ECO100468	STY100845	94%	100%	100%
ECO100468	STM100558	94%	100%	100%
ECO100468	VCH103521	69%	100%	100%
ECO100468	VCH101110	75%	100%	100%
ECO100468	YPS001600	83%	100%	100%
ECO100469	ABA105707	48%	97.3%	97.0%
ECO100469	BAN105697	24%	61.3%	85.4%
ECO100469	BAN103529	27%	63.6%	89.8%
ECO100469	BAN105257	27%	67.6%	93.7%
ECO100469	BFR10916	30%	63.8%	48.5%
ECO100469	BFR11614	32%	69.9%	50.9%
ECO100469	BBU100446	21%	69.4%	57.9%
ECO100469	BCE111018	51%	97.7%	97.5%
ECO100469	BMA106790	50%	99.3%	98.4%
ECO100469	CBO103826	23%	65.9%	91.1%
ECO100469	CDP101177	26%	90.1%	93.7%
ECO100469	EBC105058	92%	98.2%	98.4%
ECO100469	EFM201852	28%	67.9%	96.1%
ECO100469	ECO100469	100%	100%	100%
ECO100469	KPN309208	91%	100%	100%
ECO100469	MAV102680	29%	64.9%	93.2%
ECO100469	MBV104698	29%	61.5%	86.2%
ECO100469	MLP100477	27%	61.5%	86.5%
ECO100469	MTU203193	29%	61.5%	86.2%
ECO100469	PRT101586	71%	98.0%	95.4%
ECO100469	PAE205513	62%	98.0%	97.0%
ECO100469	PPU103619	33%	68.3%	64.0%
ECO100469	SPA103965	83%	98.2%	100%
ECO100469	STY100846	94%	99.6%	99.6%
ECO100469	SAU401722	23%	66.8%	85.2%
ECO100469	TPA100056	23%	37.6%	47.1%
ECO100469	YPS001597	79%	98.2%	97.3%
ECO100473	BCE112818	22%	90.5%	79.4%
ECO100473	BFU105062	27%	87.5%	92.5%
ECO100473	BMA109015	23%	55.7%	93.1%
ECO100473	CAC101805	21%	87.1%	80.6%
ECO100473	EBC101032	70%	51.1%	100%
ECO100473	ECO100473	100%	100%	100%
ECO100473	KPN305997	67%	96.2%	99.2%
ECO100473	PRT105875	47%	99.2%	97.8%
ECO100473	SPA101218	64%	100%	100%
ECO100473	STY100870	65%	100%	100%
ECO100473	VCH102186	33%	88.6%	80.2%
ECO100473	YPS001582	56%	99.2%	97.4%
ECO100475	ABA101879	41%	7.2%	16.0%
ECO100475	BAN105978	44%	57.4%	98.6%
ECO100475	BAN110321	44%	69.3%	100%
ECO100475	BFR10291	39%	86.6%	98.1%
ECO100475	BPT102136	41%	6.8%	15.8%
ECO100475	BCE110602	43%	73.5%	97.9%
ECO100475	BFU113139	47%	72.8%	81.7%
ECO100475	BMA106854	46%	73.3%	73.4%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100475	CJU101080	30%	86.9%	89.4%
ECO100475	CAC100879	39%	18.9%	7.9%
ECO100475	CBO102754	38%	99.2%	99.5%
ECO100475	CDF102644	39%	4.6%	16.2%
ECO100475	CDP100778	38%	5.2%	7.9%
ECO100475	EBC100331	89%	4.2%	19.6%
ECO100475	EFA201855	39%	19.2%	7.9%
ECO100475	EFM201092	37%	87.5%	98.5%
ECO100475	ECO100475	100%	100%	100%
ECO100475	HIN100276	37%	3.2%	10.7%
ECO100475	HPY101055	32%	88.0%	99.6%
ECO100475	KPN308679	87%	6.6%	18.6%
ECO100475	LPN101141	44%	77.7%	89.0%
ECO100475	LPN101253	45%	77.7%	88.7%
ECO100475	LMO100878	37%	1.4%	12.6%
ECO100475	MCA100406	36%	87.5%	95.5%
ECO100475	MAV100988	36%	72.9%	81.5%
ECO100475	MBV103852	44%	77.7%	79.7%
ECO100475	MLP101222	34%	87.4%	96.5%
ECO100475	MTU200960	44%	77.7%	81.9%
ECO100475	NGO100160	39%	86.7%	98.1%
ECO100475	NME201398	40%	87.2%	98.6%
ECO100475	PMU101892	39%	2.9%	10.9%
ECO100475	PRT105140	72%	27.5%	12.7%
ECO100475	PAE203917	41%	7.1%	16.3%
ECO100475	PPU108258	41%	99.6%	98.6%
ECO100475	PSY102170	42%	7.0%	21.1%
ECO100475	SPA101217	84%	86.8%	100%
ECO100475	STY100871	93%	99.9%	99.9%
ECO100475	STM104228	42%	4.4%	8.3%
ECO100475	SAU802557	38%	99.9%	99.5%
ECO100475	SEP201193	37%	7.2%	16.6%
ECO100475	SHA100292	40%	73.9%	100%
ECO100475	SMU100795	41%	4.4%	8.9%
ECO100475	SPN400641	43%	72.1%	79.3%
ECO100475	SPY201317	41%	4.6%	8.9%
ECO100475	TPA101026	34%	3.7%	9.8%
ECO100475	UUR100203	28%	76.9%	92.9%
ECO100475	VCH102181	50%	9.0%	19.3%
ECO100475	YPS001578	66%	7.3%	22.9%
ECO100485	ABA102979	44%	78.8%	90.3%
ECO100485	BPT100402	42%	86.5%	82.4%
ECO100485	BCE103660	39%	98.1%	60.3%
ECO100485	BFU101347	38%	93.3%	90.2%
ECO100485	BMA107037	42%	86.1%	81.2%
ECO100485	CAC101080	25%	84.1%	98.9%
ECO100485	CBO103052	27%	48.6%	52.1%
ECO100485	CDF104317	23%	79.3%	92.3%
ECO100485	EBC103361	92%	90.9%	100%
ECO100485	EFA202370	25%	74.0%	85.1%
ECO100485	ECO100485	100%	100%	100%
ECO100485	KPN303861	87%	100%	95.4%
ECO100485	LMO100084	26%	80.3%	96.4%
ECO100485	NGO100490	35%	75.5%	71.8%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100485	NMB201781	35%	75.5%	71.8%
ECO100485	PRT104443	57%	89.4%	97.9%
ECO100485	PAE202854	49%	91.3%	95.5%
ECO100485	PPU111360	45%	93.8%	91.2%
ECO100485	PSY100343	47%	75%	98.8%
ECO100485	SPA101077	87%	98.1%	94.9%
ECO100485	STY100879	89%	98.1%	100%
ECO100485	SPY201146	27%	84.1%	55.6%
ECO100485	VCH103503	56%	90.9%	88.8%
ECO100485	YPS001527	71%	98.1%	98.1%
ECO100488	ABA100225	26%	47.2%	31.6%
ECO100488	ABA100477	26%	27.1%	80.5%
ECO100488	BAN104847	21%	28.1%	4.3%
ECO100488	BAN109223	31%	7.2%	48.7%
ECO100488	BAN101440	31%	7.6%	43.5%
ECO100488	BAN110288	23%	20.8%	3.8%
ECO100488	BFR104422	59%	1.9%	27%
ECO100488	BCE108121	26%	28.9%	68.0%
ECO100488	BCE104951	26%	49.5%	30.5%
ECO100488	BFU107935	29%	21.0%	31.4%
ECO100488	BFU100092	51%	6.2%	98.9%
ECO100488	BFU100109	28%	9.3%	60.6%
ECO100488	BFU102581	29%	11.2%	4.4%
ECO100488	BMA107682	26%	25.9%	53.9%
ECO100488	CAC100404	28%	7.9%	39.1%
ECO100488	EBC107494	33%	21.5%	50.7%
ECO100488	EBC103412	28%	21.5%	25.6%
ECO100488	EBC104888	26%	28.5%	68.9%
ECO100488	ECO100686	77%	23.5%	70.2%
ECO100488	ECO101427	86%	41.4%	86.8%
ECO100488	ECO100683	77%	88.2%	89.3%
ECO100488	ECO103515	77%	88.2%	90.6%
ECO100488	ECO103405	74%	99.6%	99.7%
ECO100488	ECO100488	100%	100%	100%
ECO100488	MAV107400	23%	19.1%	20.6%
ECO100488	PRT103688	29%	7.3%	73.6%
ECO100488	PRT103361	31%	7.6%	75.1%
ECO100488	PRT103421	25%	11.2%	4.4%
ECO100488	PAE202682	31%	88.3%	88.8%
ECO100488	PPU107712	30%	7.6%	94.3%
ECO100488	PPU109654	27%	6.8%	73.5%
ECO100488	PPU110484	28%	12.0%	92.3%
ECO100488	PPU107101	28%	10.9%	38.6%
ECO100488	PPU109653	28%	41.0%	73.7%
ECO100488	PPU109652	25%	32.9%	38.8%
ECO100488	PPU110482	29%	53.6%	54.8%
ECO100488	PSY108533	33%	4.9%	83.6%
ECO100488	PSY101322	55%	4.1%	24.3%
ECO100488	PSY105816	47%	7.2%	45.3%
ECO100488	PSY102083	25%	44.4%	45.2%
ECO100488	SPA106438	38%	2.5%	16.8%
ECO100488	SPA100247	26%	53.2%	67.7%
ECO100488	STY104094	26%	30.2%	50.1%
ECO100488	STY104095	30%	59.5%	51.1%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100488	STM103807	42%	8.0%	50.8%
ECO100488	STM103806	26%	40.7%	49.6%
ECO100488	YPS002860	25%	84.9%	75.6%
ECO100490	ABA100225	43%	36.9%	5.8%
ECO100490	ABA100477	45%	38.6%	10.5%
ECO100490	BAN101440	31%	39.4%	37.8%
ECO100490	BAN109223	31%	39.4%	44.2%
ECO100490	BAN110288	33%	39.4%	4.4%
ECO100490	BCE104951	36%	50.4%	8.6%
ECO100490	BCE108121	46%	39.0%	10.1%
ECO100490	BFU100092	48%	36.9%	97.8%
ECO100490	BFU102581	51%	39.0%	6.1%
ECO100490	BFU100109	47%	41.1%	14.2%
ECO100490	BMA107682	35%	38.6%	8.0%
ECO100490	CAC100404	32%	35.6%	30.3%
ECO100490	EBC103412	43%	38.1%	33.2%
ECO100490	ECO100686	73%	39.8%	19.7%
ECO100490	ECO103517	66%	45.8%	45.5%
ECO100490	ECO103515	75%	39.4%	6.8%
ECO100490	ECO103405	76%	39.8%	6.7%
ECO100490	ECO100683	76%	39.4%	6.7%
ECO100490	ECO100488	80%	39.4%	6.5%
ECO100490	ECO101427	42%	92.4%	31.4%
ECO100490	ECO100490	100%	100%	100%
ECO100490	PRT103361	33%	38.6%	65.5%
ECO100490	PRT103421	45%	39.4%	7.7%
ECO100490	PAE202682	51%	39.4%	7.0%
ECO100490	PPU107712	49%	23.3%	63.2%
ECO100490	PPU107101	48%	38.6%	22.0%
ECO100490	PPU110482	46%	39.0%	6.6%
ECO100490	PPU109652	45%	40.7%	6.4%
ECO100490	PSY101322	55%	24.6%	23.9%
ECO100490	PSY105816	46%	39.0%	40.8%
ECO100490	PSY102083	47%	39.0%	5.8%
ECO100490	SPA106438	46%	37.3%	40%
ECO100490	STY104095	48%	38.6%	10.8%
ECO100490	STY104094	51%	37.3%	6.6%
ECO100490	STM103806	49%	37.7%	6.7%
ECO100490	STM103807	49%	37.7%	37.0%
ECO100490	YPS002860	47%	39.4%	6.4%
ECO100491	ECO100491	100%	100%	100%
ECO100499	ABA104957	38%	99.6%	97.3%
ECO100499	BCE100249	55%	98.4%	94.4%
ECO100499	BFU102476	53%	98.4%	95.1%
ECO100499	BFU114367	56%	98.4%	94.4%
ECO100499	ECO100499	100%	100%	100%
ECO100499	PAE201500	59%	98.4%	97.7%
ECO100499	PPU107167	57%	98.4%	97.7%
ECO100499	SPA103879	83%	100%	100%
ECO100499	STY100931	84%	100%	100%
ECO100499	STM100624	84%	100%	100%
ECO100500	ABA103985	44%	98.6%	99.0%
ECO100500	BPT100453	34%	93.5%	99.3%
ECO100500	BCE106184	65%	99.0%	97.0%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100500	BFU104727	64%	99.7%	96.0%
ECO100500	EFA200236	38%	95.9%	94.9%
ECO100500	EFM201855	40%	96.2%	95.6%
ECO100500	ECO100500	100%	100%	100%
ECO100500	HPY200581	30%	97.3%	98.6%
ECO100500	LMO101779	41%	95.9%	98.3%
ECO100500	PAE201499	62%	99.3%	98.3%
ECO100500	PPU100008	63%	99.3%	98.0%
ECO100500	SPA103880	90%	100%	100%
ECO100500	STY100932	91%	100%	100%
ECO100500	STM100645	91%	100%	100%
ECO100501	ECO100501	100%	100%	100%
ECO100501	STM104546	57%	53.3%	58.3%
ECO100502	ABA104757	29%	99.3%	89.2%
ECO100502	BCE108546	28%	98.2%	82.9%
ECO100502	BFU103203	26%	96.3%	79.2%
ECO100502	BMA100176	27%	96.3%	79.2%
ECO100502	EBC101321	30%	36.8%	93.7%
ECO100502	EFA202073	53%	97.9%	86.5%
ECO100502	ECO100502	100%	100%	100%
ECO100502	KPN301121	28%	96.8%	84.7%
ECO100502	PAE200475	30%	98.2%	74.4%
ECO100502	PPU107187	28%	96.3%	78.9%
ECO100502	PSY103157	26%	95.4%	85.9%
ECO100502	SPA103881	91%	100%	90.3%
ECO100502	STM100647	92%	100%	100%
ECO100502	YPS002040	27%	96.8%	85.4%
ECO100522	EBC104095	61%	93.5%	100%
ECO100522	ECO100522	100%	100%	100%
ECO100522	LPN101710	27%	35.2%	30.8%
ECO100522	PRT104641	26%	77.4%	75.5%
ECO100522	PRT103064	29%	92.2%	95.5%
ECO100522	PRT105670	29%	98.3%	97.8%
ECO100522	PRT105544	30%	95.7%	98.6%
ECO100522	PRT105082	33%	93.5%	95.9%
ECO100522	PRT101027	42%	97.0%	96.9%
ECO100522	PRT101728	46%	96.1%	94.0%
ECO100522	PRT105207	46%	93.0%	93.0%
ECO100522	SPA101492	64%	96.5%	93.7%
ECO100522	STY101296	62%	99.6%	99.6%
ECO100522	STM101010	61%	99.6%	99.6%
ECO100523	BBU100344	26%	17.1%	36.2%
ECO100523	BMA102682	37%	95.0%	95.5%
ECO100523	CDF100539	22%	18.0%	56.5%
ECO100523	EBC104108	65%	95.6%	99.3%
ECO100523	ECO100523	100%	100%	100%
ECO100523	KPN201537	39%	95.8%	98.7%
ECO100523	MAV108170	24%	20.3%	37.6%
ECO100523	PRT104636	44%	97.5%	99.3%
ECO100523	SPA103196	72%	68.5%	100%
ECO100523	STY101297	69%	98.6%	98.5%
ECO100523	STM101011	70%	98.6%	98.5%
ECO100523	SAU300377	26%	11.5%	52.7%
ECO100541	EBC101703	52%	98.4%	95.4%



Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100541	ECO100541	100%	100%	100%
ECO100541	PRT105258	53%	48.8%	98.4%
ECO100541	PRT100296	49%	96.9%	93.2%
ECO100541	YPS000017	65%	94.5%	93.0%
ECO100549	ECO100549	100%	100%	100%
ECO100554	ABA101274	33%	40.6%	26.5%
ECO100554	ABA101204	39%	31.7%	23.0%
ECO100554	ABA104217	29%	37.8%	27.6%
ECO100554	BFR101004	32%	28.9%	11.4%
ECO100554	BFR105341	35%	31.3%	13.8%
ECO100554	BCE106065	29%	29.7%	67.3%
ECO100554	BCE113842	31%	49.8%	33.2%
ECO100554	BMA107995	26%	31.3%	22.3%
ECO100554	BMA105539	32%	31.7%	38.9%
ECO100554	ECO101470	28%	92.4%	89.7%
ECO100554	ECO103438	36%	93.6%	96.3%
ECO100554	ECO100554	100%	100%	100%
ECO100554	LPN103151	28%	32.9%	24.5%
ECO100554	MBV100183	26%	55.4%	37.6%
ECO100554	MTU301482	26%	55.4%	36.9%
ECO100554	NME102614	33%	29.7%	24.6%
ECO100554	PRT101349	35%	39.8%	39.5%
ECO100554	PRT104740	34%	51.8%	48.0%
ECO100554	PAE202094	29%	33.3%	25%
ECO100554	PAE203213	31%	30.5%	22.6%
ECO100554	PPU102277	25%	37.8%	26.4%
ECO100554	PPU101064	31%	30.5%	21.5%
ECO100554	SPA100934	36%	50.6%	51.4%
ECO100554	SPA103838	40%	49.8%	40.1%
ECO100554	STY102368	37%	49.0%	48.6%
ECO100554	STY102403	33%	73.9%	64.9%
ECO100554	STM103734	40%	49.8%	40.1%
ECO100554	SMU100002	29%	37.8%	27.9%
ECO100554	VCH100823	29%	49.0%	44.2%
ECO100555	BFU112796	28%	18.3%	36.0%
ECO100555	EBC102973	48%	100%	97.1%
ECO100555	ECO100555	100%	100%	100%
ECO100555	LPN101913	38%	97.8%	98.7%
ECO100555	PPU103428	23%	56.8%	38.8%
ECO100555	SPA103146	46%	100%	100%
ECO100555	STY101101	46%	100%	100%
ECO100555	YPS000286	40%	91.5%	90.4%
ECO100557	ABA102872	22%	69.9%	59.8%
ECO100557	ECO100557	100%	100%	100%
ECO100557	PPU111671	33%	99.3%	98.9%
ECO100557	PSY102041	25%	73.3%	70.7%
ECO100560	BAN106854	24%	24.4%	90.1%
ECO100560	BAN112348	33%	23.8%	76.5%
ECO100560	BAN100221	25%	74.8%	77.7%
ECO100560	BAN103717	26%	62.5%	96.9%
ECO100560	BAN100334	26%	57.1%	93.3%
ECO100560	BAN102939	26%	74.8%	76.4%
ECO100560	BAN113334	25%	63.5%	84.6%
ECO100560	BAN102333	27%	68.8%	71.4%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100560	BAN110951	28%	62.5%	67.8%
ECO100560	BFR10765	27%	59.6%	63.9%
ECO100560	BFR103543	27%	64.0%	68.4%
ECO100560	BPT104047	31%	97.9%	96.7%
ECO100560	BCE114206	31%	97.9%	97.4%
ECO100560	BFU111283	42%	61.7%	63.6%
ECO100560	BFU103037	32%	97.7%	98.6%
ECO100560	BMA100332	31%	98.3%	98.1%
ECO100560	CAC102666	28%	60.6%	62.2%
ECO100560	CDF100992	28%	52.7%	65.7%
ECO100560	EBC104519	56%	99.8%	97.8%
ECO100560	ECO100560	100%	100%	100%
ECO100560	KPN302405	66%	98.5%	98.3%
ECO100560	LPN102226	32%	63.3%	88.0%
ECO100560	LMO102551	24%	99.8%	98.6%
ECO100560	PAE202808	41%	68.3%	72.7%
ECO100560	PPU101821	35%	97.7%	98.4%
ECO100560	PPU101984	35%	97.9%	96.4%
ECO100560	PSY104285	40%	67.3%	70.9%
ECO100560	SAU801414	23%	95%	96.5%
ECO100560	YPS003206	35%	67.1%	69.3%
ECO100572	ECO100572	100%	100%	100%
ECO100572	ECO100016	100%	100%	100%
ECO100572	ECO102351	100%	100%	99.5%
ECO100572	KPN301837	28%	24.6%	33.5%
ECO100572	KPN301756	28%	24.6%	25.9%
ECO100572	PPU112458	31%	21.6%	17.3%
ECO100572	PPU110183	31%	21.6%	18.0%
ECO100572	PPU100534	31%	21.6%	17.3%
ECO100572	PPU111918	31%	21.6%	17.3%
ECO100572	PPU111424	31%	21.6%	17.3%
ECO100572	PPU109580	31%	21.6%	17.3%
ECO100572	STY100108	28%	24.6%	25.9%
ECO100582	BAN107042	36%	24.8%	26.5%
ECO100582	BAN100797	25%	61.9%	58.9%
ECO100582	BAN107954	22%	56.0%	61.5%
ECO100582	BAN107919	23%	84.3%	79.6%
ECO100582	CAC102393	22%	47.5%	43.3%
ECO100582	CDF102033	25%	37.7%	36.8%
ECO100582	EBC100468	78%	74.8%	100%
ECO100582	EFA205322	25%	90.6%	88.1%
ECO100582	ECO100582	100%	100%	100%
ECO100582	KPN304825	84%	96.2%	96.2%
ECO100582	PRT102496	24%	69.8%	63.2%
ECO100582	PAE204156	41%	97.8%	98.0%
ECO100582	SPA102125	76%	100%	100%
ECO100582	STY101372	79%	100%	100%
ECO100582	SHA100136	24%	88.4%	86.1%
ECO100582	SPY200281	22%	81.4%	76.5%
ECO100582	VCH100763	36%	96.5%	92%
ECO100582	YPS002778	53%	92.1%	86.9%
ECO100584	ABA103671	56%	98.5%	98.7%
ECO100584	BAN111652	41%	98.7%	99.8%
ECO100584	BAN104146	48%	98.7%	98.1%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100584	BCE105183	43%	65.1%	93.5%
ECO100584	EBC100728	73%	81.9%	100%
ECO100584	ECO100584	100%	100%	100%
ECO100584	KPN304829	81%	98.7%	98.9%
ECO100584	MAV100968	42%	98.7%	96.7%
ECO100584	MBV101299	37%	97.4%	95.3%
ECO100584	MTU202348	39%	97.4%	93.6%
ECO100584	PAE204226	46%	98.7%	96.7%
ECO100584	PSY105284	42%	90.7%	92.5%
ECO100584	SPA100882	82%	99.6%	100%
ECO100584	STY101374	85%	99.6%	99.4%
ECO100584	STM101106	86%	99.6%	99.6%
ECO100584	VCH100759	48%	98.5%	98.0%
ECO100584	YPS002354	42%	93.7%	95.0%
ECO100593	EBC102628	50%	99%	99.3%
ECO100593	ECO100593	100%	100%	100%
ECO100593	KPN303370	48%	97.7%	94.2%
ECO100593	SPA103039	53%	99.3%	99.3%
ECO100593	STY101394	54%	99.3%	99.3%
ECO100619	EBC101386	61%	100%	83.9%
ECO100619	ECO100619	100%	100%	100%
ECO100619	KPN302688	50%	100%	89.3%
ECO100619	SPA102530	61%	100%	100%
ECO100619	STY101451	68%	100%	83.9%
ECO100632	ABA105508	56%	99.5%	99.1%
ECO100632	BAN102826	43%	99.3%	99.5%
ECO100632	BFR10298	34%	99.5%	99.9%
ECO100632	BPT102350	48%	99.8%	99.9%
ECO100632	BBU100250	38%	99.5%	99.6%
ECO100632	BCE103321	49%	99.9%	100%
ECO100632	BMA109061	49%	99.9%	94.6%
ECO100632	CJU101017	43%	99.4%	99.6%
ECO100632	CPN200606	41%	99.5%	99.9%
ECO100632	CTR200474	40%	99.5%	99.9%
ECO100632	CAC101070	40%	99.0%	99.1%
ECO100632	CBO100961	40%	98.8%	99.0%
ECO100632	CDF103555	44%	99.4%	99.5%
ECO100632	CDP101454	36%	99.0%	97.1%
ECO100632	EBC100539	92%	55.2%	100%
ECO100632	EFA200538	42%	99.3%	99.5%
ECO100632	EFM200610	43%	99.3%	99.5%
ECO100632	ECO100632	100%	100%	100%
ECO100632	HIN100900	72%	99.9%	99.8%
ECO100632	HPY101524	42%	98.8%	99.3%
ECO100632	KPN300581	97%	18.4%	96.3%
ECO100632	KPN302684	95%	99.8%	100%
ECO100632	LPN103327	54%	100%	100%
ECO100632	LMO100611	42%	99.3%	99.5%
ECO100632	MCA102972	49%	99.7%	99.0%
ECO100632	MAV103767	37%	96.3%	90.9%
ECO100632	MBV104696	37%	96.2%	92.8%
ECO100632	MLP100028	36%	99.9%	97.7%
ECO100632	MTU200041	37%	96.2%	93.0%
ECO100632	MGE100272	34%	99.4%	99.6%

Query LocusID	Homolog LocusID	Identity	Query Coverage	Homolog Coverage
ECO100632	MPN100453	34%	99.4%	99.5%
ECO100632	NGO100059	57%	99.9%	99.8%
ECO100632	NME200518	55%	99.9%	100%
ECO100632	PMU101214	72%	99.8%	99.8%
ECO100632	PRT102887	80%	100%	100%
ECO100632	PAE203984	57%	99.8%	99.8%
ECO100632	PPU108817	57%	99.8%	99.8%
ECO100632	PSY105072	57%	99.8%	99.8%
ECO100632	SPA100430	93%	58.6%	98.8%
ECO100632	STY101466	95%	100%	100%
ECO100632	SAU801760	42%	99.3%	99.5%
ECO100632	SEP202121	42%	99.3%	99.5%
ECO100632	SHA100631	42%	99.3%	99.5%
ECO100632	SMU100492	40%	99.4%	99.5%
ECO100632	SPN400235	42%	99.4%	99.5%
ECO100632	SPY200128	42%	99.4%	99.5%
ECO100632	TPA100579	39%	98.8%	99.2%
ECO100632	UUR100373	34%	99.4%	99.9%
ECO100632	VCH100940	75%	99.8%	95.7%
ECO100632	YPS001199	84%	100%	100%
ECO100645	ABA101420	41%	99.0%	100%
ECO100645	BPT102527	46%	98.3%	96.7%
ECO100645	BCE104111	65%	100%	99%
ECO100645	BFU109692	45%	99.0%	85.4%
ECO100645	BMA102165	72%	86.8%	100%
ECO100645	EBC102933	91%	100%	100%
ECO100645	ECO100645	100%	100%	100%
ECO100645	KPN300407	91%	41.7%	100%
ECO100645	KPN302708	89%	100%	100%
ECO100645	PRT102877	75%	100%	100%
ECO100645	PAE201341	58%	97.4%	97.7%
ECO100645	PPU101496	57%	96.4%	97.4%
ECO100645	PSY105194	55%	96.4%	94.8%
ECO100645	SPA102587	95%	92.1%	100%
ECO100645	STY101796	93%	100%	98.1%
ECO100645	YPS001209	78%	100%	100%
ECO100647	ABA104991	36%	96.5%	92.3%
ECO100647	BPT100972	30%	94.1%	98.1%
ECO100647	BBU100236	28%	32.4%	32.1%
ECO100647	BCE102700	33%	92.2%	82.3%
ECO100647	BFU103489	32%	95.9%	92.9%
ECO100647	BMA107358	31%	70.3%	97.8%
ECO100647	CJU101021	23%	53.7%	55.1%
ECO100647	CPN200092	23%	95.3%	92.1%
ECO100647	CTR200810	28%	35.2%	34.9%
ECO100647	CAC101602	24%	29.7%	62.6%
ECO100647	CDP101117	24%	81.6%	90.6%
ECO100647	EBC102934	85%	99.6%	100%
ECO100647	ECO100647	100%	100%	100%
ECO100647	HIN100288	44%	97.1%	95.4%
ECO100647	HPY100177	23%	60.5%	66.8%
ECO100647	KPN302711	83%	100%	100%
ECO100647	LPN102781	30%	84.6%	98.6%
ECO100647	MCA100961	36%	96.3%	94.9%